PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

#15

In re U.S. Patent No.: 4,254,129

Filed: April 10, 1979

Issued: March 3, 1981

Title: Piperidine Derivatives

RECEIVED

SEP 05 1996

PATENT EXTENSION
A/C PATENTS

Inventors: Albert A. Carr; Joseph E. Dolfini; George J. Wright

I hereby certify that this correspondence is being deposited with the United States Postal Service as Express Mail in an envelope addressed to Assistant Commissioner for Patents, Washington, D.C. 20231, on

4 September 1996
Date of Deposit

Janet Grubb
Signature

EM312458882US
Express Mail No.

TRANSMITTAL LETTER

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

Transmitted herewith are (1) an Application for Extension of the Patent Term under 35 U.S.C. § 156 for U.S. Patent No. 4,254,129, including Appendices A through I and including a Declaration of Patent Owner, (2) a certified duplicate of the Application for Extension of the Patent Term under 35 U.S.C. § 156 for U.S. Patent No. 4,254,129, including Appendices A through I and including a Declaration of Patent Owner, (3) an Information Disclosure Statement regarding the Application for Extension of the Patent Term under 35 U.S.C. § 156 for U.S. Patent No. 4,254,129, and (4) a Power of Attorney and Establishing Right of Assignee to Take Action for U.S. Patent No. 4,254,129.

The Commissioner is hereby authorized to charge any fees under 35 U.S.C. 156(h), including the $1060.00 fee established by 37 C.F.R. § 1.20(j), which may be required by the papers filed herewith, or to credit any overpayment, to Account No. 13-2764. Two duplicate copies of this Transmittal Letter are enclosed.

Respectfully submitted,

Louis J. Wille, Reg. No. 32,954
Attorney/Agent for Applicant

Hoechst Marion Roussel, Inc.
2110 East Galbraith Road
P. O. Box 156300
Cincinnati, Ohio 45215-6300
Telephone (513) 948-6354
Telefax (513) 948-7961
(513) 948-4681

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23088 111 1,060.00CH

M00956 US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re U.S. Patent No.:
4,254,129

Issued: **March 3, 1981**

Filed: **April 10, 1979**

Title: **Piperidine Derivatives**

Inventors: Albert A. Carr; Joseph E. Dolfini; George J. Wright

Examiner: Norma Milestone

Art Unit: 121

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TRANSMITTAL OF INFORMATION DISCLOSURE STATEMENT
FOR WHICH THE FEE SPECIFIED UNDER 37 C.F.R. 1.97(c) IS REQUIRED

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Enclosed is an Information Disclosure Statement for which the fee specified in 37 C.F.R. 1.97(c) is required.

Please charge Deposit Account No. **13-2764** in the amount of $220.00. Two duplicate copies of this sheet are enclosed. The Commissioner is authorized to charge any fees under 37 C.F.R. 1.17(p) or credit any overpayment to Account No. **13-2764**.

Respectfully submitted,

Louis J. Wille
Attorney/Agent for Applicant

Hoechst Marion Roussel, Inc.
2110 East Galbraith Road
P. O. Box 156300
Cincinnati, Ohio 45215-6300
Telephone (513) 948-6354
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Docket No. M00956 US

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PATENT EXTENSION
AND PATENTS

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In re U.S. Patent No. 4,254,129

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INFORMATION DISCLOSURE STATEMENT UNDER 37 C.F.R.1.765

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

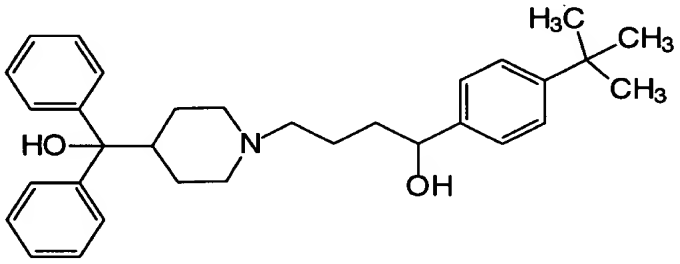
Applicant submits herewith patents, publications, and/or other information of which it is aware, which it believes may be material, as defined in 37 C.F.R. 1.765(a), to the examination of this Application for Extension of Patent Term and in respect of which there may be a duty to disclose in accordance with 37 C.F.R. 1.765. While the information referred to in this Information Disclosure Statement may be material pursuant to 37 C.F.R. 1.765, the filing of this Information Disclosure Statement is not intended to constitute an admission that any patent, publication or other information referred to is, or is considered to be, material to the determinations to be made in the patent term extension proceeding. The filing of this Information Disclosure Statement shall not be construed to mean that a search has been made or that no other material information exists.

OTHER INFORMATION

(1) Relationship Between Fexofenadine Hydrochloride and Seldane™:

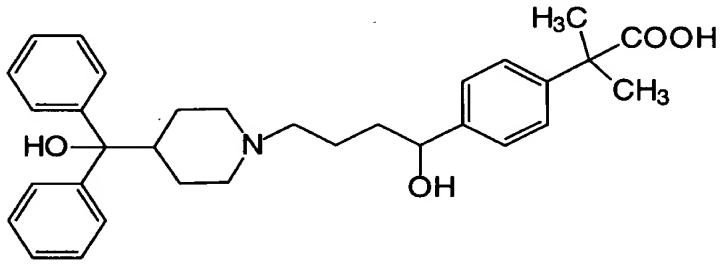
Seldane™ is an FDA approved drug (NDA 18-949) which was initially approved and made commercially available in the U.S. in 1985 and was the first of a new generation of non-sedating

antihistamines. The active ingredient of Seldane™ is terfenadine which is α-[4-(1,1-dimethylethyl)phenyl]-4-(hydroxydiphenylmethyl)-1-piperidinebutanol and has the following chemical structure:



Terfenadine

As indicated in the Seldane™ Prescribing Information as of January 1995, which is enclosed herewith [PHYSICIAN'S DESK REFERENCE, 50th Edition, 1996, Medical Economics Company, Montvale, New Jersey 07645-1742, pages 1536-38], terfenadine is a histamine H_1-receptor antagonist which undergoes extensive first pass metabolism to two primary metabolites, an active acid metabolite and an inactive dealkylated metabolite. The active acid metabolite bears a dimethylbenzeneacetic acid substituent in the place of the dimethylethylphenyl substituent of terfenadine and has the following chemical structure:



Active Acid Metabolite/Fexofenadine

The active acid metabolite is the same basic chemical structure as fexofenadine which, as the hydrochloride salt, is the active ingredient of Allegra™ (NDA 20-625) and the drug product for which the Application for Extension of Patent Term is submitted herewith. It is now known that the active acid metabolite is the agent primarily responsible for the antihistaminic activity of Seldane™. U.S. Patent No. 4,254,129 (the '129 patent) is listed in the Seldane™ NDA in accordance with 21 U.S.C. § 355(b)(1) and is noticed on the Prescribing Information for Seldane™. The '129 patent is

also listed in the Allegra™ NDA in accordance with 21 U.S.C. § 355(b)(1) and will be noticed on the Prescribing Information for Allegra™.

(2) **Terfenadine Patent Infringement Suits Involving U.S. Patent No. 4,254,129 and Seldane™:**

The '129 patent is the subject of patent infringement suits against various prospective generic suppliers of Seldane™ under a theory of Inducement of Infringement. Basically, a patient who ingests a generic copy of Seldane™ makes and uses the active acid metabolite. The generic supplier is therefore inducing infringement of claims 1, 6, 8 and 11 of the '129 patent and is liable as an infringer under 35 U.S.C. § 271(b). All of these suits are currently pending. The following is a listing of the various suits alleging infringement of the '129 patent (the defendants in all such suits having filed Paragraph (iv) Patent Certifications under the provisions of the 1984 Drug Price Competition and Patent Term Extension Act):

A. Marion Merrell Dow Inc. et al. v. Baker-Norton Pharmaceuticals, Inc., United States District Court, Southern District of Florida, Case No. 94-1245-CV-Lenard; this is a patent infringement suit against a prospective supplier of a generic version of Seldane™;

B. Marion Merrell Dow, Inc. v. Geneva Pharmaceuticals, Inc., United States District Court, District of Colorado, Civil Action No. 94-N-495; this is a patent infringement suit against a prospective supplier of a generic version of Seldane™;

C. Hoechst Marion Roussel, Inc. v. Par Pharmaceutical, Inc., United States District Court, District of New Jersey, Civil Action No. 95-3673(DRD); this is a patent infringement suit against a prospective supplier of a generic version of Seldane™;

D. Hoechst Marion Roussel, Inc. et al. v. Novopharm Limited, United States District Court, District of Maryland, Civil Action No. MJG-96-236; this is a patent infringement suit against a prospective supplier of a generic version of Seldane™.

(3) Other Litigation Involving U.S. Patent No. 4,254,129 and Seldane™:

Other litigation actions relevant to the '129 patent include the following:

A. Hoechst Marion Roussel, Inc. v. David A. Kessler, M.D., et al., United States District Court, District of Columbia Circuit, Civil Action No. 95-5397; this suit involves the legal effect of listing the '129 patent in the Seldane™ NDA; was decided in favor of Hoechst Marion Roussel, Inc., with the District Court issuing a permanent injunction; an appeal by FDA to United States Court of Appeals for the District of Columbia Circuit is currently pending; Mylan Pharmaceuticals, Inc., and Mutual Pharmaceutical Company, Inc., have been denied the right to intervene in this action but have been granted the right to file briefs as amicus curiae;

B. Mutual Pharmaceutical Company, Inc. v. Hoechst Marion Roussel, Inc., United States District Court, Eastern District of Pennsylvania, Civil Action No. 96-1409; this is an antitrust suit brought by Mutual concerning the listing of the '129 patent in the Seldane™ NDA; this suit also includes a patent infringement counterclaim against Mutual as a prospective supplier of a generic version of Seldane™; Mutual has filed an ANDA for a generic version of Seldane™ but has not filed a Patent Certification Notice.

(4) Citizen's Petition Involving ALLEGRA™:

A Citizen's Petition was filed with FDA on May 17, 1996, requesting FDA to change its policy and declare that the drug product fexofenadine hydrochloride is not entitled to a 5 year ANDA exclusivity. The Citizen's Petition of May 17, 1996, and the Response by Hoechst Marion Roussel, Inc. of August 12, 1996, are enclosed herewith.

REMARKS

Fexofenadine hydrochloride and the active acid metabolite are covered by claims 1, 6, 8 and 11 of the '129 patent which is the subject patent for which the Application for Extension of Patent Term is submitted herewith. Claims 1, 6, and 8 of the '129 patent claim compounds per se regardless of the manner in which they are made, i.e., synthetically or metabolically. Thus, claims 1, 6 and 8 of the '129 patent claim fexofenadine hydrochloride and the active acid metabolite as compounds per se.

Claim 11 of the '129 patent claims a method of treating allergic reactions by administering certain compounds including the active acid metabolite or fexofenadine. One way to administer a compound included within the scope of claim 11 is by oral ingestion of a bioavailable formulation of the drug product fexofenadine hydrochloride as in Allegra™. Another way to administer a compound included within the scope of claim 11 is by oral ingestion of a bioavailable formulation of terfenadine as in Seldane™ wherein the terfenadine is metabolized by the patient *in vivo* to the active acid metabolite. Thus, claim 11 of the '129 patent claims a method of using Allegra™, as well as a method of using Seldane™. The '129 patent has never been the subject of an Application for Extension of Patent Term based upon Seldane™ or the drug product terfenadine.

Since claim 11 of the '129 patent covers a method of using Seldane™ as one means of administering a compound included within the scope of the claim, and could reasonably be asserted if a person not licensed by the owner engaged in the manufacture or sale of Seldane™ to a patient who would ingest the Seldane™, the '129 patent is listed in the Seldane™ NDA in accordance with 21 U.S.C. § 355(b)(1).

Since claims 1, 6, 8 and 10 of the '129 patent claim the drug product fexofenadine hydrochloride which is the active ingredient of Allegra™, and since claim 11 of the '129 patent claims a method of administering fexofenadine hydrochloride to treat allergic reactions, and since these claims could reasonably be asserted if a person not licensed by the owner engaged in the manufacture, use or sale of Allegra™, the '129 patent is listed in the Allegra™ NDA in accordance with 21 U.S.C. § 355(b)(1).

Although the active acid metabolite of terfenadine has been made metabolically by patients who have ingested Seldane™ since its approval in 1985, the FDA approval of Allegra™ on 25 July 1996 was the first permitted marketing or use of the product fexofenadine hydrochloride under 21 U.S.C. § 355(b)(1) and therefore the '129 patent which covers fexofenadine hydrochloride is eligible for a patent term extension[1].

[1] The requirements for eligibility for patent term extension under 35 U.S.C. § 156(a) for a patent which claims a human drug product or method of using a human drug product are (1) the term of the patent has not expired before an application for extension of patent term is submitted; (2) the term of the patent has never been extended under 35 U.S.C. § 156(e)(1); (3) an application for extension is submitted by the owner of record of the patent and in accordance with the requirements for the application under 35 U.S.C. § 156(d)(1) through (4); (4) the product has been subject to a regulatory review period before its commercial marketing or use; and (5) the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred.

35 U.S.C. § 156(a) provides that in order for a human drug product to be eligible for a patent term extension, "the permission for the commercial marketing or use of the product after such regulatory review period is the first permitted commercial marketing or use of the product under the provision of law under which such regulatory review period occurred". 35 U.S.C. § 156(a)(5)(A). The term "product" is defined in 35 U.S.C. § 156(f)(1) as meaning a "drug product" which is further defined under 35 U.S.C. § 156(f)(2) as meaning the "active ingredient of ... a new drug ... including any salt or ester of the active ingredient, as a single entity or in combination with another active ingredient". *Id.* at 156(f)(2) [emphasis added].

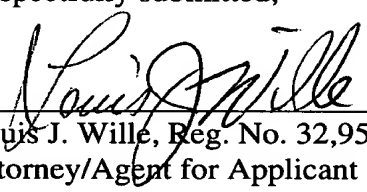
The phrase "active ingredient of ... a new drug" has a plain and unambiguous meaning as a constituent element of a mixture or compounds. As such, an active ingredient of a new drug must be found in the dosage form prior to dosing and not merely something which can be derived from that found in the dosage form or from which an ingredient of the dosage form can be derived. For example, in Glaxo Operations UK Ltd. v. Quigg, 13 USPQ2d 1628 (1990, Fed Cir.), the CAFC construed the term "active ingredient" as it is used in 35 U.S.C. § 156(f)(2) and affirmed the district court finding that the statute is plain and unambiguous. The district court found that an active ingredient "must be something found in the mixture or compound, not just something that can be derived from it or from which the mixture or compound can be derived". Glaxo Operations UK Ltd. v. Quigg, 10 USPQ2d 1100 (1989, E.D.Va) at 1103. In rebutting the Commissioner's argument that the term "active ingredient" includes the ultimate therapeutic agent as well, the district court stated that

> [T]his rationale is untenable, its flaw manifest. The statute says "ingredient", not "moiety". And, as noted, an "ingredient" must be present in the drug product when administered.

Id. at 1103. The active ingredient of Allegra™ as defined for purposes of 35 U.S.C. § 156 is fexofenadine hydrochloride and any salts or esters thereof. The active ingredient of Seldane™ as similarly defined is terfenadine and any salts or esters thereof. Fexofenadine is not a salt or ester of terfenadine, but bears a dimethylbenzene acetic acid substituent in the place of the dimethylethylphenyl substituent of terfenadine. Neither fexofenadine hydrochloride nor any of its salts or esters have been approved for commercial marketing or use by FDA under 21 U.S.C. § 355 prior to the 25 July 1996 approval for Allegra™. The FDA approval of Allegra™ on 25 July 1996 was the first permitted marketing or use of the product fexofenadine hydrochloride under 21 U.S.C. §

355 and therefore the '129 patent which covers fexofenadine hydrochloride is elegible for a patent term extension under 35 U.S.C. § 156.

Respectfully submitted,



Louis J. Wille, Reg. No. 32,954
Attorney/Agent for Applicant

Hoechst Marion Roussel, Inc.
2110 East Galbraith Road
P. O. Box 156300
Cincinnati, Ohio 45215-6300
Telephone (513) 948-6354
Telefax (513) 948-7961
(513) 948-4681

FORM PTO-1449 (Modified)	U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE	ATTY. DOCKET NO.	SERIAL NO.	PATENT NO.
INFORMATION DISCLOSURE STATEMENT BY APPLICANT		M00956	07/28,813	4,254,129
(Use several sheets if necessary)		APPLICANT: A.A. Carr et al		
		FILING DATE: April 10, 1979	ISSUE DATE: March 3, 1981	GROUP: 121

U.S. PATENT DOCUMENTS

EXAMINER INITIALS	*		DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPRORIATE

FOREIGN PATENT DOCUMENTS

EXAMINER INITIALS	*		DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	TRANSLATION YES	TRANSLATION NO

OTHER DOCUMENTS

EXAMINER INITIALS	*		AUTHOR, TITLE, DATE, PERTINENT PAGES, ETC.
			Physician's Desk Reference, 50th Edition, 1996, Medical Economics Company, Montvale, New Jersey 07645-1742, pp 1536-38
			Citizen's Petition of May 17, 1996, "Citizen Petition--Eligibility of Fexofenadine For Five-Year Exclusivity" (11 pages)
			Hoechst Marion Roussel, Inc. Response of August 12, 1996 to "Citizen Petition--Eligibility of Fexofenadine For Five-Year Exclusivity" (6 pages)

EXAMINER	DATE CONSIDERED

EXAMINER: Initial if citation considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.
Note: Asterisk (*) item(s) have been previously cited in a related application(s) either by the applicant or by the USPTO and therefore copies of the reference(s) are not being submitted.

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of
A.A. Carr, J.E. Dolfini, George J. Wright

Examiner: Norma Milestone

Art Unit: 121

Patent No.: **4,254,129**

Issued: **March 3, 1981**

Title: **Piperidine Derivatives**

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Signature

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REVOCATION/APPOINTMENT OF POWER OF ATTORNEY
OR AUTHORIZATION OF AGENT

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

I hereby revoke all previous powers of attorney or authorization of agents in the above identified application.

I/we hereby appoint the following person(s) as my/our attorney(s) or agent(s) to prosecute said application, and to transact all business in the Patent and Trademark Office connected therewith:

Louis J. Wille, Reg. No. 32,954
Stephen L. Nesbitt, Reg. No. 28,981
Gary D. Street, Reg. No. 25,611

Change the correspondence address and direct all future correspondence to:
Hoechst Marion Roussel, Inc.
2110 East Galbraith Road
P. O. Box 156300
Cincinnati, Ohio 45215-6300

I am the Assignee of record of the entire interest. Certification under 37 CFR 3.73(b) is enclosed.

Respectfully submitted,

Stephen L. Nesbitt
CorporatePatent Counsel

Telephone (513) 948-7965
Telefax (513) 948-7961
(513) 948-4681

Docket No. M00956 US

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of
A.A. Carr
J.E. Dolfini
George J. Wright

Examiner: Norma Milestone

Art Unit: 121

Patent No. 4,254,129

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CERTIFICATE UNDER 37 CFR 3.73(b)
ESTABLISHING RIGHT OF ASSIGNEE TO TAKE ACTION

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

1) The assignee(s) of the entire right, title and interest hereby seek(s) to take action in the PTO in this manner.

IDENTIFICATION OF ASSIGNEE

2) Merrell Pharmaceuticals Inc. (name of assignee)
Corporation (type of assignee, e.g., corporation, partnership, university, government agency, etc.)

PERSON AUTHORIZED TO SIGN

3) Stephen L. Nesbitt, Corporate Patent Counsel

I, the person signing below, aver that I am empowered to sign this statement on behalf of the assignee.

BASIS OF ASSIGNEE'S INTEREST

A chain of title from the inventor(s) to the current assignee as shown below:

1) From: Albert A. Carr, Joseph E. Dolfini, George J. Wright
To: Richardson-Merrell Inc. Recorded October 16, 1980, Reel 3806, Frame 572 & 573

2) From: Richardson-Merrell Inc.
To: Merrell Dow Pharmaceuticals Inc. (Name Change Recordal submitted on August 15, 1996)

3) From: Merrell Dow Pharmaceuticals Inc.
To: Merrell Pharmaceuticals Inc. (Name Change Recordal submitted on August 15, 1996)

COPIES OF DOCUMENTS IN CHAIN OF TITLE

Copies of the assignments(s) or other document(s) in the chain of title are attached as follows:

Copy of Recorded Assignment

Copy of the Name Change Recordal from Richardson-Merrell Inc. to Merrell Dow Pharmaceuticals Inc.

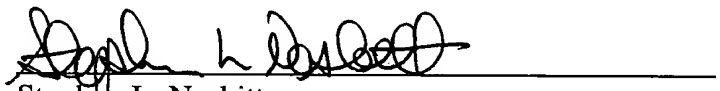
Copy of the Name Change Recordal from Merrell Dow Pharmaceuticals Inc. to Merrell Pharmaceuticals Inc.

DECLARATIONS

I, the undersigned, have reviewed all the documents in the chain of title of the patent matter identified above, and to the best of my knowledge and belief, title is in the assignee identified above.

I, hereby declare that all statements made herein of my own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both, under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Respectfully submitted,



Stephen L. Nesbitt
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DECLARATION OF PATENT OWNER

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

Louis J. Wille, authorized patent attorney for the Applicant, Merrell Pharmaceuticals Inc., submits this declaration as required by 37 C.F.R. § 1.740, along with an Application for Extension of Patent Term for U.S. Patent No. 4,254,129, and hereby declares THAT:

(1) I am a patent attorney authorized to practice before the U.S. Patent and Trademark Office and have general authority from the owner of U.S. Patent No. 4,254,129 to act on its behalf in regard to patent matters;

(2) I have reviewed and understand the contents of the enclosed Application for Extension of Patent Term for U.S. Patent No. 4,254,129;

(3) I believe that U.S. Patent No. 4,254,129 is subject to an Extension of Patent Term pursuant to 37. C.F.R. § 1.710;

(4) I believe a Patent Term Extension of 677 days for U.S. Patent No. 4,254,129 is justified under 35 U.S.C. § 156 and the applicable regulations related thereto;

(5) I believe that U.S. Patent No. 4,254,129 meets the conditions for extension of term as set forth in 37 C.F.R. § 1.720; and

(6) all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Title 18, United States Code § 1001, and that such willful false statements may jeopardize the validity of the application for extension or any patent extended thereon.

Louis J. Wille, Reg. No. 32,954
Attorney/Agent for Applicant

Hoechst Marion Roussel, Inc.
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APPLICATION FOR EXTENSION OF PATENT TERM PURSUANT TO 35 U.S.C. § 156

Assistant Commissioner for Patents

Washington, D.C. 20231

Sir:

Merrell Pharmaceuticals Inc., as the owner of record of U.S. Patent No. 4,254,129, hereby submits this application for Extension of Patent Term pursuant to 35 U.S.C. § 156. The Applicant requests that the term of U.S. Patent No. 4,254,129 be extended for 677 days in accordance with 35 U.S.C. § 156 and that this extended term be added to the GATT recalculated expiration date of 10 April 1999 in accordance with applicable U.S. law so as to expire on 15 February 2001.

OWNER OF RECORD

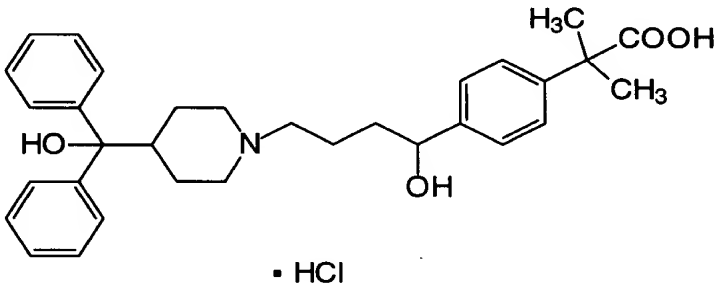
The original assignee of U.S. Patent No. 4,254,129, the subject of the instant Application for Extension of Patent Term, was Richardson-Merrell Inc. As evidenced by the Certificate of Merger of Dow Merger Sub Incorporated into Richardson-Merrell Inc. of 10 March 1981 (attached hereto as Appendix A), Richardson Merrell Inc. merged with Dow Merger Sub Incorporated and changed its name as the surviving corporation to Merrell Dow Pharmaceuticals Inc.. As evidenced by the Certificate of Amendment to the Certificate of Incorporation of Merrell Dow Pharmaceuticals Inc. of 22 September 1995 (attached hereto as Appendix B), Merrell Dow Pharmaceuticals Inc. changed its name to Merrell Pharmaceuticals Inc.. Merrell Pharmaceuticals Inc. is a wholly owned subsidiary of Hoechst Marion Roussel, Inc..

The Certificate of Merger of 10 March 1981 and the Certificate of Amendment of 22 September 1995 have been duly filed in the U.S. Patent Office by Express Mail with certificate of mailing on 15 August 1996.

The numbered sections below correspond to the specific requirements for an Application for Extension of Patent Term as set forth in 37 C.F.R. § 1.740(a) (1)-(17).

(1) IDENTIFICATION OF THE APPROVED PRODUCT

The Drug Product which is the subject of the instant Application for Extension of Patent Term is fexofenadine hydrochloride, the active ingredient of Allegra™ (fexofenadine hydrochloride capsules 60 mg). Fexofenadine hydrochloride is a histamine H_1-receptor antagonist with the following chemical structure:



The chemical name of fexofenadine hydrochloride is 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α,α-dimethyl benzeneacetic acid hydrochloride.

(2) IDENTIFICATION OF FEDERAL STATUTE

Pursuant to 21 U.S.C. § 355(a), "[N]o person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) or (j) is effective with respect to such drug".

As a new drug product for human use, fexofenadine hydrochloride was subjected to regulatory review by the U.S. Food and Drug Administration ("FDA") pursuant to 21 U.S.C. § 355 (b)(1) which is also cited as Section 505(b)(1) of the Federal Food, Drug and Cosmetic Act. Thus, regulatory review and approval by the FDA was required for marketing fexofenadine hydrochloride in the U.S. Pursuant to this statute, fexofenadine hydrochloride was the subject of a New Drug Application (NDA 20-625) for which numerous clinical trials were conducted under an Investigational New Drug (IND) filing.

(3) IDENTIFICATION OF DATE OF APPROVAL UNDER FEDERAL STATUTE

By letter of 25 July 1996, attached as Appendix C, FDA issued to Hoechst Marion Roussel, Inc., an approval for marketing Allegra™ (fexofenadine hydrochloride capsules 60mg). FDA concluded that, based upon review of the NDA, "adequate information has been presented to demonstrate that the drug product is safe and effective for the relief of symptoms associated with seasonal allergic rhinitis". Page 1 of 25 July 1996 Letter from FDA to Hoechst Marion Roussel, Inc. (Appendix C).

(4) IDENTIFICATION OF ACTIVE INGREDIENT

The active ingredient in Allegra™ for which regulatory approval was obtained from FDA is fexofenadine hydrochloride or 4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α,α-dimethyl benzeneacetic acid hydrochloride as indicated by the Prescribing Information approved by FDA for Allegra™ attached in Appendix D.

The drug product fexofenadine hydrochloride, including any salt or ester thereof, has not been previously approved for commercial marketing or use under the Federal Food, Drug and Cosmetic Act either as a single entity or in combination with any other active ingredient.

(5) STATEMENT AS TO 60 DAY WINDOW

The instant Application for Extension of Patent Term of U.S. Patent No. 4,254,129 for fexofenadine hydrochloride has been submitted within the 60 day period permitted for submission pursuant to 37 C.F.R. § 1.720(f). The last day for submission of the instant Application is 60 days from 25 July 1996 or 23 September 1996.

(6) IDENTIFICATION OF PATENT

The instant Application relates to the following Patent:

U.S. Patent No. 4,254,129

Inventors: Albert A. Carr; Joseph E. Dolfini; George J. Wright

Date Issued: March 3, 1981

Expiration Date: April 10, 1999 (GATT recalculated expiration date)

(7) COPY OF PATENT

A copy of U.S. Patent No. 4,254,129 is attached in Appendix E.

(8) COPY OF DISCLAIMER, CERTIFICATE OF CORRECTION, ETC.

With respect to U.S. Patent No. 4,254,129, which is the subject of the instant application, no disclaimer, certificate of correction, or reexamination certificate has been issued or filed. Maintenance fee payments were not required since U.S. Patent No. 4,254,129 was filed prior to 12 December 1980.

(9) STATEMENT REGARDING PATENT CLAIMS AND SHOWING

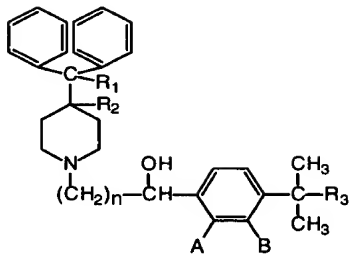
The Patent which is the subject of the instant Application for Extension of Patent Term (U.S. Patent No. 4,254,129) claims the approved product fexofenadine hydrochloride and the approved method of using said approved product. The applicable claims are Claims 1, 6, 8, 10 and 11.

The following analysis identifies the applicable claims of U.S. Patent No. 4,254,129 and demonstrates the manner in which each applicable claim reads on the approved product or approved method of use:

Claim 1

Claim 1 reads as follows:

1. A compound of the formula



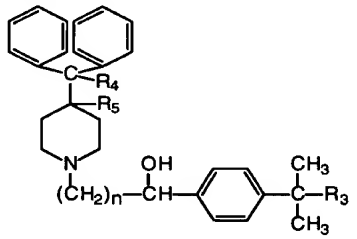
wherein R_1 represents hydrogen or hydroxy; R_2 represents hydrogen; or R_1 and R_2 taken together form a second bond between the carbon atoms bearing R_1 and R_2; n is an integer of from 1 to 5; R_3 is -COOH or -COOalkyl wherein the alkyl moiety has from 1 to 6 carbon atoms and is straight or branched; each of A and B is hydrogen or hydroxy; with the proviso that at least one of A or B is hydrogen; and pharmaceutically acceptable salts and individual optical isomers thereof.

Claim 1 is a generic composition of matter claim which includes fexofenadine hydrochloride within its scope wherein R_1 is hydroxy, R_2 is hydrogen, n is 3, R_3 is -COOH, A is hydrogen, and B is hydrogen.

Claim 6

Claim 6 reads as follows:

6. A compound of claim 1 of the formula



wherein R_4 is hydroxy and R_5 is hydrogen, or R_4 and R_5 taken together form a second bond between the carbon atoms bearing R_4 and R_5; n is the integer 3; and R_3 is -COOH or a pharmaceutically acceptable salt thereof.

Claim 6 is a generic composition of matter claim which includes fexofenadine hydrochloride within its scope wherein R_4 is hydroxy and R_5 is hydrogen.

Claim 8

Claim 8 reads as follows:

8. A compound of claim 1 which is 4-[4-[-4-(hydroxydiphenylmethyl)-1-piperidinyl]-1-hydroxybutyl]-α, α-dimethylbenzeneacetic acid or a pharmaceutically acceptable salt thereof.

Claim 8 is a composition of matter claim which specifically claims fexofenadine and pharmaceutically acceptable salts thereof, including a hydrochloride salt.

Claim 10

Claim 10 reads as follows:

> 10. A pharmaceutical composition in unit dosage form comprising an effective antiallergic amount of a compound of claim 1 and a significant amount of a pharmaceutically acceptable carrier.

Claim 10 is a generic composition of matter claim which includes the approved drug ALLEGRA™ (fexofenadine hydrochloride 60mg capsules) within its scope. Fexofenadine hydrochloride is a compound of claim 1 as indicated above which is available as ALLEGRA™ in the unit dosage form of a capsule. 60 mg of fexofenadine hydrochloride is an effective antiallergic amount of fexofenadine hydrochloride as evidenced by the FDA approved Prescribing Information (attached hereto in Appendix D) wherein fexofenadine hydrochloride 60 mg capsules was approved for use in the relief of symptoms associated with seasonal allergic rhinitis. The approved capsule formulation contains a significant amount of pharmaceutically acceptable carriers including croscarmellose sodium, gelatin, lactose, microcrystalline cellulose, and pregelatinized starch, as evidenced by the FDA approved Prescribing Information (attached hereto in Appendix D).

Claim 11

Claim 11 reads as follows:

> 11. A method of treating allergic reactions in a patient in need thereof which comprises administering to said patient an effective amount of a compound of claim 1.

Claim 11 is a generic method of use claim which includes within its scope the FDA approved use of ALLEGRA™. Fexofenadine hydrochloride is a compound of claim 1 as indicated above. Oral administration of ALLEGRA™ (fexofenadine hydrochloride, 60 mg capsules) is one way to provide an effective amount of fexofenadine hydrochloride for the relief of symptoms associated with seasonal allergic rhinitis as evidenced by the FDA approved Prescribing Information (attached hereto in Appendix D).

(10) STATEMENT REGARDING RELEVANT DATES

The following are relavant dates and information for a determination of the applicable regulatory review period pursuant to 35 U.S.C. § 156:

a. IND number and Effective date:
Fexofenadine hydrochloride is the subject of IND No. 43,573 which was submitted on 4 October 1993 and received by FDA on 5 October 1993 as evidenced by the FDA Acknowledgement Letter attached hereto as Appendix F. The IND became effective 30 days after receipt by FDA pursuant to 21 C.F.R. § 312.40(b)(1) or on 4 November 1993.

b. NDA Number and Initial Submission Date:
Fexofenadine hydrochloride is the subject of NDA 20-625 which was initially submitted to FDA on 31 July 1995 as evidenced by the Letter to FDA Accompanying the NDA Submission attached hereto as Appendix G.

c. NDA Approval Date:
NDA 20-625 was approved by FDA on 25 July 1996 as evidenced by the FDA Approval Letter attached hereto as Appendix C.

(11) DESCRIPTION OF SIGNIFICANT ACTIVITIES DURING REGULATORY REVIEW PERIOD

a. Significant Activities During IND Period:

During the IND Period from 4 November 1993 to 31 July 1995, Applicant conducted extensive clinical trials both in the U.S. and in foreign countries in over two thousand patients designed to demonstrate the safety and efficacy of fexofenadine hydrochloride in the treatment of seasonal allergic rhinitis. A brief summary of various clinical trials conducted with the approved drug product (ALLEGRA™; fexofenadine hydrochloride capsules 60 mg) together with applicable start and completion dates and a brief description of these studies is attached hereto as Table of Clinical Trials in Appendix H. In addition to these activities, various other activities were also conducted during this time period including, for example, manufacturing regulatory compliance, various non-clinical studies designed to support safety and efficacy, and the like.

b. Significant Activities During the NDA Period:

During the NDA Period from 31 July 1995 to 25 July 1996, Applicant corresponded extensively with the FDA concerning follow-up activities and questions or requests by FDA concerning the NDA. In addition to these activities, various other activities were also conducted during this time period including, for example, safety update reports, annual summary for the NDA, and the like. A brief description of some of the significant communications with FDA concerning the drug product fexofenadine hydrochloride during this period is attached hereto as a Chronological Listing of Significant Communications in Appendix I.

(12) STATEMENT OF ELIGIBILITY, LENGTH OF EXTENSION AND METHOD OF DETERMINATION

In the opinion of Applicant, U.S. Patent No. 4,254,129 (the '129 patent) is eligible for a Patent Term Extension pursuant to 35 U.S.C. § 156(a) for the following reasons:

(1) the '129 patent claims the drug product fexofenadine hydrochloride and its method of use in treating seasonal allergic rhinitis;

(2) the term of the '129 patent has not expired prior to the submission of the instant Application for Extension of Term;

(3) the term of the '129 patent has never been extended under 35 U.S.C. § 156;

(4) the instant Application for Extension of Patent Term has been submitted in accordance with 35 U.S.C. § 156 (d)(1) through (4);

(5) the drug product fexofenadine hydrochloride, which is the active ingredient of Allegra™, was subject to regulatory review pursuant to 21 U.S.C. § 355(b)(1) prior to its approval by FDA for commercial marketing on 25 July 1996; and

(6) the FDA approval for commercial marketing on 25 July 1996 was the first permitted commercial marketing or use of the drug product fexofenadine hydrochloride, including any salt or ester thereof as a single entity or in combination with another active ingredient, under 21 U.S.C. § 355.

Applicant believes that the proper length of the Patent Term Extension for U.S. Patent No. 4,254,129 pursuant to 35 U.S.C. § 156 due to the regulatory review period for the drug product fexofenadine hydrochloride is 677 days which, when added to the expiration date of the patent, would extend the expiration date of U.S. Patent No. 4,254,129 to 15 February 2001.

The Patent Term Extension was calculated pursuant to 37 C.F.R. § 1.775 as follows:

a. The Regulatory Review Period was calculated as the sum of the IND period and the NDA period as follows:

The IND period began on the date the IND became effective (30 days after receipt of the IND by FDA). Receipt of the IND was on 5 October 1993 and the effective date of the IND was therefore 30 days later on 4 November 1993. The IND period ended on the date the NDA was submitted to FDA on 31 July 1995. The time period from 4 November 1993 to 31 July 1995 is 634 days.

The NDA period began on the date the NDA was submitted to FDA on 31 July 1995 and ended on the date the FDA approved the NDA on 25 July 1996. The time period from 31 July 1995 to 25 July 1996 is 360 days.

The Regulatory Review Period is the sum of the IND period (634 days) and the NDA period (360 days). Therefore, the Regulatory Review Period is 994 days.

b. The Patent Term Extension Period was calculated by adjusting the Regulatory Review Period as follows:

(i) subtracting the number of days within the Regulatory Review Period which were on and before the date on which the patent issued: Since the '129 patent issued on 10 April 1979, no days within the Regulatory Review Period are on or before the date on the the patent issued. Therefore, 0 days were subtracted;

(ii) subtracting the number of days within the Regulatory Review Period during which Applicant did not act with due diligence: Applicant believes that due diligence was pursued during the entire Regulatory Review Period. Therefore, 0 days were subtracted;

(iii) subtracting one-half the number of days in the IND period from the Regulatory Review Period: One-half of the IND Period of 634 days is 317 days. This is subtracted from the Regulatory Review Period of 994 days to yield 677 days as the applicable Patent Term Extension Period.

c. The Extended Term Expiration Date of U.S. Patent No. 4,254,129 is calculated as follows:

The Patent Term Extension Period of 677 days is added to the expiration date of 10 April 1999 (GATT recalculated expiration date) in accordance with applicable U.S. law to give an Extended Term Expiration Date of 15 February 2001.

d. The 14 Year Cap Date is calculated as follows:

14 years was added to the date of NDA approval on 25 July 1996 to yield a 14 Year Cap Date of 25 July 2010.

e. The 5 Year Cap Date is calculated as follows:

Since the '129 patent was issued prior to 24 September 1984 and no request for exemption for the drug product fexofenadine hydrochloride was submitted under subsection (i) of section 505 or subsection (d) of section 507 of the Federal Food, Drug and Cosmetic Act prior to 24 September 1984, 5 years is added to the expiration date of the patent (10 April 1999) to yield a 5 Year Cap Date of 10 April 2004.

f. Patent Term Extension Expiration Date for U.S. Patent No. 4,254,129 is calculated as follows:

Since the Extended Term Expiration Date of 15 February 2001 as calculated in (c) above is the earlier date in comparison to the 14 Year Cap Date as calculated in (d) above, and since the Extended Term Expiration Date of 15 February 2001 as calculated in (c) above is the earlier date in comparison to the 5 Year Cap Date as calculated in (e) above, the appropriate Patent Term Extension Expiration Date for U.S. Patent 4,254,129 is 15 February 2001.

(13) ACKNOWLEDGEMENT OF DUTY TO DISCLOSE

Applicant hereby acknowledges pursuant to 35 U.S.C. § 156(d)(4) and 37 C.F.R. § 1.765 a duty to disclose to the Commissioner of Patents and Trademarks and the Secretary of Health and Human Services any information which is material to the determination of entitlement to the extension sought hereunder.

Applicant has submitted herewith an Information Disclosure Statement to the Commissioner of Patents and Trademarks.

(14) PRESCRIBED FEE

The prescribed fee for receiving and acting upon this Application for Patent Term Extension including that required by 37 C.F.R. § 1.20(j) is authorized by the Transmittal Letter which accompanies the instant Application.

(15) CORRESPONDENCE CONTACT

Please direct inquiries and correspondence related to the instant Application to the undersigned at the address below.

(16) DUPLICATE COPIES

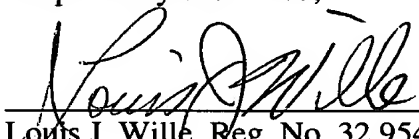
Applicant has submitted two copies of this Application in the form of certified duplicates.

(17) DECLARATION

A Declaration of Patent Owner as required by 37 C.F.R. § 1.740(a)(17) and § 1.740(b) has been submitted herewith.

Applicant awaits early notification of a favorable decision granting the requested Patent Term Extension.

Respectfully submitted,



Louis J. Wille, Reg. No. 32,954
Attorney/Agent for Applicant

Hoechst Marion Roussel, Inc.
2110 East Galbraith Road
P. O. Box 156300
Cincinnati, Ohio 45215-6300
Telephone (513) 948-6354
Telefax (513) 948-7961

A

Our Reference: M00956
Serial No. 07/28,813
Patent No. 4,254,129
Issue Date: March 3, 1981

INDEX OF APPENDICES

A. Certificate of Merger of 10 March 1981

B. Certificate of Amendment of 22 September 1995

C. FDA Letter of 25 July 1996 Approving Allegra™ for Commercial Marketing

D. Prescribing Information for Allegra™

E. Copy of U.S. Patent No. 4,254,129

F. FDA Letter of 7 October 1993 Acknowledging IND Submission

G. MMD Letter of 31 July 1995 Accompanying NDA Submission

H. Table of Controlled Clinical Trials, Clinical Pharmacology Studies, and Biopharmaceutics Studies

I. Chronological Listing of Significant Communications after NDA Submission

State of DELAWARE

Office of SECRETARY OF STATE

I, Glenn C. Kenton *Secretary of State of the State of Delaware, do hereby certify* that the "Richardson-Merrell Inc.", filed a Certificate of Merger, changing its corporate title to "Merrell Dow Pharmaceuticals Inc.", on the tenth day of March, A.D. 1981, at 11:15 o'clock A.M.

In Testimony Whereof, *I have hereunto set my hand and official seal at Dover this* tenth *day of* March *in the year of our Lord one thousand nine hundred and* eighty-one.

Glenn C. Kenton

Glenn C. Kenton, Secretary of State

CERTIFICATE OF MERGER

of

DOW MERGER SUB INCORPORATED

into

RICHARDSON-MERRELL INC.

UNDER SECTION 251 OF THE GENERAL CORPORATION LAW OF THE STATE OF DELAWARE

Pursuant to Section 251(c) of the General Corporation Law of the State of Delaware, Richardson-Merrell Inc., a Delaware corporation ("RMI"), hereby certifies the following information relating to the merger of Dow Merger Sub Incorporated, a Delaware corporation ("Dowsub"), with and into RMI (the "Merger").

1. The names and states of incorporation of RMI and Dowsub, which are the constituent corporations in the Merger (the "Constituent Corporations"), are:

Name	State
Richardson-Merrell Inc.	Delaware
Dow Merger Sub Incorporated	Delaware

2. The Agreement and Plan of Reorganization, dated as of November 1, 1980, as amended February 4, 1981, by and among RMI, Dowsub and The Dow Chemical Company, a Delaware corporation (the "Merger Agreement"), setting forth the terms and conditions of the Merger, has been approved, adopted, certified, executed and acknowledged by each of the Constituent Corporations in accordance with the provisions of Section 251(c) of the General Corporation Law of the State of Delaware.

3. The name of the corporation surviving the Merger is Richardson-Merrell Inc. which shall, at the Effective Time, be named "Merrell Dow Pharmaceuticals Inc."

4. Pursuant to the Merger Agreement, the Certificate of Incorporation of RMI in effect immediately prior to the Effective Time of the Merger (as defined in the Merger Agreement) shall be the Certificate of Incorporation of the surviving corporation; provided, however, that:

(a) Article FIRST of such Certificate shall be amended at the Effective Time to read in its entirety *in haec verba:* "The name of the corporation is Merrell Dow Pharmaceuticals Inc. (hereinafter sometimes called the 'Corporation')"; and

(b) Article FOURTH of such Certificate shall be amended at the Effective Time to read in its entirety *in haec verba:* "The total number of shares of all classes of stock which the Corporation shall have authority to issue is 1,000, and all 1,000 shares shall consist of Common Stock, par value $.10 per share."

5. An executed Merger Agreement is on file at the principal place of business of the surviving corporation, which is located at 2110 East Galbraith Road, Cincinnati, Ohio 45215.

6. A copy of the Merger Agreement will be furnished by the surviving corporation, on request and without cost, to any stockholder of either of the Constituent Corporations.

IN WITNESS WHEREOF, this Certificate of Merger has been executed on this 10th day of March, 1981.

RICHARDSON-MERRELL INC.

By H S Richardson
Chairman of the Board

[CORPORATE SEAL]

Attest:

John Gunther
Secretary

State of Delaware

Office of the Secretary of State

I, EDWARD J. FREEL, SECRETARY OF STATE OF THE STATE OF DELAWARE, DO HEREBY CERTIFY THE ATTACHED IS A TRUE AND CORRECT COPY OF THE CERTIFICATE OF AMENDMENT OF "MERRELL DOW PHARMACEUTICALS INC.", CHANGING ITS NAME FROM "MERRELL DOW PHARMACEUTICALS INC." TO "MERRELL PHARMACEUTICALS INC.", FILED IN THIS OFFICE ON THE TWENTY-SECOND DAY OF SEPTEMBER, A.D. 1995, AT 10 O'CLOCK A.M.

Edward J. Freel, Secretary of State

0326521 8100

950225229

AUTHENTICATION: 7660645

DATE: 10-02-95

9-22-95

CERTIFICATE OF AMENDMENT TO CERTIFICATE OF INCORPORATION OF MERRELL DOW PHARMACEUTICALS INC.

The undersigned, Richard J. Markham, President and Chief Executive Officer, and Rebecca R. Tilden, Secretary of Merrell Dow Pharmaceuticals Inc., a corporation organized and existing under the laws of the State of Delaware (hereinafter sometimes referred to as the "Corporation"), do hereby certify as follows:

FIRST: That the Board of Directors of the Corporation duly proposed the following amendment to the Certificate of Incorporation of the Corporation, duly adopted a resolution setting forth the proposed amendment, subject to approval of the shareholder of the Corporation:

> **RESOLVED,** that the Certificate of Incorporation of Merrell Dow Pharmaceuticals Inc., a Delaware corporation, (the "Certificate of Incorporation"), shall be, and it hereby is, amended by deleting all of paragraph 1 thereof and by inserting, in lieu thereof, a new paragraph 1 providing in its entirety as follows:
>
> **FIRST:** The name of the corporation is MERRELL PHARMACEUTICALS INC. (hereinafter sometimes called the "Corporation").

SECOND: That by Statement of Unanimous Consent the shareholder of the Corporation voted in favor of the amendment and that said amendment was duly adopted.

THIRD: That the capital of the Corporation will not be reduced under or by reason of said amendment.

FOURTH: That, accordingly, the amendments to the Certificate of Incorporation of Merrell Dow Pharmaceuticals Inc., as hereinbefore set forth in Article FIRST of this Certificate of Amendment, has been duly adopted in accordance with the provisions of Section 242 of the General Corporation Law of the State of Delaware.

IN WITNESS WHEREOF, we, Richard J. Markham, President and Chief Executive Officer, and Rebecca R. Tilden, Secretary of Merrell Dow Pharmaceuticals Inc., Inc., have signed this Certificate under the corporate seal of the Corporation (thereby acknowledging, under penalties of perjury, that the

foregoing instrument is their act and deed and that the facts stated therein are true) on the 15th day of September, 1995.

Merrell Dow Pharmaceuticals Inc.

Richard J. Markham
President and Chief Executive Officer

(CORPORATE SEAL)

ATTEST:

Rebecca R. Tilden, Secretary

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-625

JUL 25 1996

Hoechst Marion Roussel, Inc.
P.O. Box 9627
Kansas City, MO 64134-0627

Attention: Elaine Waller, Pharm.D.
Vice President,
U.S. Regulatory Affairs

RECEIVED AUG 0 5 1996

Dear Dr. Waller:

Reference is made to your July 31, 1995, new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Allegra (fexofenadine hydrochloride) Capsules, 60 mg.

We acknowledge receipt of your amendments dated September 5 and 27, October 6, 16, and 19, November 20 and 30, and December 8, 13, 21, and 22, 1995, January 19 and 26, February 9, 12, and 15, March 1, April 12, 26, and 29, May 2, 9, 10, 15, and 31, June 3, 4, 6, 7, 14, 18, 20, 21, and 26, and July 2 and 9, 1996.

We have completed the review of this application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for the relief of symptoms associated with seasonal allergic rhinitis as recommended in the enclosed marked-up draft physician labeling. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed marked-up draft physician labeling, and the June 26, 1996, final printed carton and container labels. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug. All labels and labeling should be revised at the next printing, or within six months, whichever occurs first, to read "Allegra (fexofenadine hydrochloride) Capsules," remove the letters "BID" in association with the name, and include the moisture statement as amended on July 9, 1996.

Please submit 16 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this

submission should be designated "FPL for approved NDA 20-625." Approval of this submission by FDA is not required before it is used.

Should additional information relating to the safety and effectiveness of the drug become available, revision of the labeling may be required.

In addition, please submit three copies of the introductory promotional material that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please send one copy to the Division of Pulmonary Drug Products and two copies of both the promotional material and the package insert directly to:

Food and Drug Administration
Division of Drug Marketing, Advertising, and Communications, HFD-40
5600 Fishers Lane
Rockville, Maryland 20857

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

We remind you of your agreement to perform full acceptance testing of the drug substance annually, and to add the statement "Protect from excessive moisture" to the packaging for aluminum foil blister packs printed after July 9, 1996. In addition, you are encouraged to characterize the mechanism of drug interaction between fexofenadine and ketoconazole and between fexofenadine and erythromycin, and to quantify the extent of any drug interaction between fexofenadine and other macrolide antibiotics, other azole antifungal agents, or cimetidine.

Please submit one market package of the drug product when it is available.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Ms. Gretchen Strange
Project Manager
(301) 827-1058

Sincerely yours,

James Bilstad, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

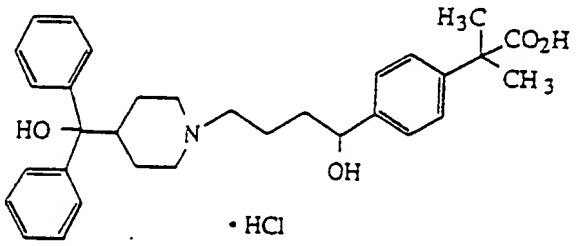
Enclosure

Prescribing Information as of July 1996

ALLEGRA™
(fexofenadine hydrochloride) Capsules
60 mg ~~capsules~~

DESCRIPTION

Fexofenadine hydrochloride, the active ingredient of ALLEGRA™, is a histamine H_1- receptor antagonist with the chemical name (±)-
4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α,α-
dimethyl benzeneacetic acid hydrochloride, (Refs. 3-9). It has the following chemical structure (Ref. 10):



The molecular weight is 538.13 (Ref. 11) and the empirical formula is $C_{32}H_{39}NO_4 \cdot HCl$ (Ref. 12). Fexofenadine hydrochloride is a white to off-white crystalline powder (Ref. 13). It is freely soluble in methanol and ethanol, slightly soluble in chloroform and ~~in~~ water, and insoluble in hexane (Ref. 14). Fexofenadine hydrochloride is ~~provided as~~ a racemate and exists as a zwitterion in aqueous media at physiological pH (Refs. 15,16).

ALLEGRA™ is formulated as capsules for oral administration (Ref. 1). Each capsule contains 60 mg fexofenadine hydrochloride and the following excipients: croscarmellose sodium, gelatin, lactose, microcrystalline cellulose, and pregelatinized starch. The printed capsule shell is made from gelatin, iron oxide, silicon dioxide, sodium lauryl sulfate, titanium dioxide and other ingredients (Ref. 2).

CLINICAL PHARMACOLOGY

Mechanism of Action

Fexofenadine, a metabolite of terfenadine, is an antihistamine with selective peripheral H_1-receptor antagonist activity (Refs. 3-8). Fexofenadine inhibited antigen-induced bronchospasm in sensitized guinea pigs and ~~inhibited~~ histamine release from peritoneal mast cells in rats (Refs. 17,18). In laboratory animals, no anticholinergic or alpha$_1$-adrenergic-receptor blocking effects were observed (Refs. 4,19,20). Moreover, no sedative or other central nervous system effects were observed (Refs. 3,21). Radiolabeled tissue distribution studies in rats indicated that fexofenadine does not cross the blood-brain barrier (Ref. 35).

Pharmacokinetics

Fexofenadine hydrochloride was rapidly absorbed following oral administration of a single dose of two 60-mg capsules to healthy male volunteers with a mean time to maximum plasma concentration occurring at 2.6 hours postdose (Ref. 31). After administration of a single dose of 60-mg as an oral solution to healthy subjects, the mean plasma concentration was 209 ng/mL (Ref. 32). Mean steady-state peak plasma concentrations of 286 ng/mL were observed when healthy volunteers were administered multiple doses of fexofenadine hydrochloride (60 mg oral solution every 12 hours for 10 doses) (Ref. 32). Fexofenadine pharmacokinetics were linear for oral doses up to 120 mg twice daily (Ref. 32). Although the absolute bioavailability of fexofenadine hydrochloride capsules is unknown, the capsules are bioequivalent to an oral solution (Ref. 31). The mean elimination half-life of fexofenadine was 14.4 hours following administration of 60 mg, twice daily, to steady-state in normal volunteers (Ref. 32).

Human mass balance studies documented a recovery of approximately 80% and 11% of the [^{14}C] fexofenadine hydrochloride dose in the feces and urine, respectively. Approximately 5% of the total dose was metabolized (Refs. 33,34). Because the absolute bioavailability of fexofenadine hydrochloride has not been established, it is unknown if the fecal component represents unabsorbed drug or the result of biliary excretion.

The pharmacokinetics of fexofenadine hydrochloride in seasonal allergic rhinitis patients were similar to those in healthy subjects. Peak fexofenadine plasma concentrations were similar between adolescent (12-16 years of age) and adult patients (Ref. 24).

Fexofenadine is 60% to 70% bound to plasma proteins, primarily albumin and α_1-acid glycoprotein (Refs. 36,37).

Special Populations

Special population pharmacokinetics (for age and renal and hepatic impairment), obtained after a single dose of 80 mg fexofenadine hydrochloride, were compared to those from normal subjects in a separate study of similar design (Ref. 38). While subject weights were relatively uniform between studies, these special population patients were substantially older than the healthy, young volunteers. Thus, an age effect may be confounding the pharmacokinetic differences observed in some of the special populations.

Effect of Age. In older subjects (≥65 years old), peak plasma levels of fexofenadine were 99% greater than those observed in normal volunteers (<65 years old). Mean elimination half-lives were similar to those observed in normal volunteers (Refs. 38,41).

Renally Impaired. In patients with mild (creatinine clearance 41-80 mL/min) to severe (creatinine clearance 11-40 mL/min) renal impairment, peak plasma levels of fexofenadine were 87% and 111% greater, respectively, and mean elimination half-lives were 59% and 72% longer, respectively, than observed in normal volunteers. Peak plasma levels in patients on dialysis (creatinine clearance ≤10 mL/min) were 82% greater and half-life was 31% longer than observed in normal volunteers. Based on increases in bioavailability and half-life, a dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function. (See DOSAGE AND ADMINISTRATION.) (Refs. 38,40)

Hepatically Impaired. The pharmacokinetics of fexofenadine hydrochloride in patients with hepatic disease did not differ substantially from that observed in healthy subjects (Refs. 38,39).

Effect of Gender. Across several trials, no clinically significant gender-related differences were observed in the pharmacokinetics of fexofenadine (Refs. 38,74).

Pharmacodynamics

Wheal and Flare. Human histamine skin wheal and flare studies following single and twice daily doses of 20 mg and 40 mg fexofenadine hydrochloride demonstrated that the drug exhibits an antihistamine effect by 1 hour, achieves maximum effect at 2-3 hours, and an effect is still seen at 12 hours (Refs. 22,23). There was no evidence of tolerance to these effects after 28 days of dosing (Ref. 23).

Effects on QTc. In dogs, (10 mg/kg/day, orally for 5 days) and rabbits (10 mg/kg intravenously over one hour) fexofenadine did not prolong QTc at plasma concentrations ~~which~~ that were at least 28 and 63 times, respectively, the therapeutic plasma concentrations in man (based on a 60 mg twice daily fexofenadine hydrochloride dose) (Refs. 24-26). No effect was observed on calcium channel current, delayed K^+ channel current or action potential duration in guinea pig myocytes, Na^+ current in rat neonatal myocytes, or on the delayed rectifier K^+ channel cloned from human heart at concentrations up to 1×10^{-5} M of fexofenadine. This concentration was at least 32 times the therapeutic plasma concentration in man (based on a 60 mg twice daily fexofenadine hydrochloride dose) (Refs. 24,27).

No statistically significant increase in mean QTc interval compared to placebo was observed in 714 seasonal allergic rhinitis patients (Ref. 73) given fexofenadine hydrochloride capsules in doses of 60 mg to 240 mg twice daily for two weeks or in 40 healthy volunteers (Ref. 29) given fexofenadine hydrochloride as an oral solution at doses up to 400 mg twice daily for 6 days (Refs. 28,29).

Clinical Studies

In three, ~~two~~ week, multi-center, randomized, double-blind, placebo-controlled trials in patients 12-68 years of age with seasonal allergic rhinitis (n=1634), fexofenadine hydrochloride 60 mg twice daily significantly reduced total symptom scores (the sum of the individual scores for sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes) compared to placebo (Refs. 75,76). Statistically significant reduction in symptom scores ~~was~~ were observed following the first 60 mg dose, with the effect maintained throughout the 12-hour interval (Ref. 77). In general, there was no additional reduction in total symptom scores with higher doses of fexofenadine up to 240 mg twice daily (Ref. 42). Although the number of subjects in some of the subgroups was small, there ~~was~~ were no significant differences in the effect of fexofenadine hydrochloride across subgroups of patients defined by gender, age and race (Ref. 45). Onset of action for reduction in total symptom scores, excluding nasal congestion, was observed at 60 minutes compared to placebo following a single 60 mg fexofenadine hydrochloride dose administered to patients with seasonal allergic rhinitis who were exposed to ragweed pollen in an environmental exposure unit (Ref. 43).

INDICATIONS AND USAGE

ALLEGRA™ is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 12 years of age and older. Symptoms treated effectively include sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes (Refs. 7,8,46,47).

CONTRAINDICATIONS

ALLEGRA™ is contraindicated in patients with known hypersensitivity to any of its ingredients.

PRECAUTIONS

Drug Interactions

In two separate studies, fexofenadine hydrochloride 120 mg twice daily (twice the recommended dose) was co-administered with erythromycin 500 mg every 8 hours or ketoconazole 400 mg once daily under steady-state conditions to normal, healthy volunteers (n=24, each study). No differences in adverse events or QTc interval were observed when subjects were administered fexofenadine hydrochloride alone or in combination with erythromycin or ketoconazole. The findings of these studies are summarized in the following table:

Effects on Steady-State Fexofenadine Pharmacokinetics After 7 Days of Co-Administration with Fexofenadine Hydrochloride 120 mg Every 12 Hours (twice recommended dose) in Normal Volunteers (n=24)

Concomitant Drug	$C_{max,ss}$ *(Peak plasma concentration)*	$AUC_{ss}(0\text{-}12h)$ *(Extent of systemic exposure)*
Erythromycin (500 mg every 8 hrs)	+82%	+109%
Ketoconazole (400 mg once daily)	+135%	+164%

The mechanisms of these interactions are unknown, and the potential for interaction with other azole antifungal or macrolide agents has not been studied (Refs. 48,49). These changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials. Fexofenadine had no effect on the pharmacokinetics of erythromycin or ketoconazole (Refs. 48,49).

Carcinogenesis, Mutagenesis, Impairment of Fertility

~~Fexofenadine is an active acid metabolite of terfenadine.~~ The carcinogenic potential and reproductive toxicity of fexofenadine hydrochloride were assessed using terfenadine studies with adequate fexofenadine exposure (based on plasma area-under-the-curve [AUC] values). No evidence of carcinogenicity was observed when mice and rats were given daily oral doses of 50 and 150 mg/kg of terfenadine for 18 and 24 months, respectively; these doses resulted in plasma AUC values of fexofenadine that were up to four times the human therapeutic value (based on a ~~60-mg~~ twice-daily fexofenadine hydrochloride dose) (Refs. 50,51).

In in-vitro (Bacterial Reverse Mutation, CHO/HGPRT Forward Mutation and Rat Lymphocyte Chromosomal Aberration assays) and in-vivo (Mouse Bone Marrow Micronucleus assay) tests, fexofenadine hydrochloride revealed no evidence of mutagenicity (Refs. 53-56).

In rat fertility studies, dose-related reductions in implants and increases in postimplantation losses were observed at oral doses equal to or greater than 150 mg/kg of terfenadine; these doses produced plasma AUC values of fexofenadine that were equal to or greater than three times the human therapeutic value (based on a 60-mg twice-daily fexofenadine hydrochloride dose) (Ref. 52).

Pregnancy

Teratogenic Effects: Category C. There was no evidence of teratogenicity in rats or rabbits at oral terfenadine doses up to 300 mg/kg; these doses produced fexofenadine plasma AUC values that were up to 4 and 37 times the human therapeutic value (based on a 60-mg twice-daily fexofenadine hydrochloride dose), respectively (Refs. 57-59).

There are no adequate and well-controlled studies in pregnant women. Fexofenadine hydrochloride should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects. Dose-related decreases in pup weight gain and survival were observed in rats exposed to oral doses equal to and greater than 150 mg/kg of terfenadine; at these doses the plasma AUC values of fexofenadine were equal to or greater than 3 times the human therapeutic values (based on a 60-mg twice-daily fexofenadine hydrochloride dose) (Ref. 52).

Nursing Mothers

There are no adequate and well-controlled studies in women during lactation. Because many drugs are excreted in human milk, caution should be exercised when fexofenadine hydrochloride is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of ALLEGRA™ in pediatric patients under the age of 12 years have not been established. Across well-controlled clinical trials in patients with seasonal allergic rhinitis, a total of 205 patients between the ages of 12 to 16 years received doses ranging from 20 mg to 240 mg twice daily for up to two weeks. Adverse events were similar in this group compared to patients above the age of 16 years (Ref. 72).

Geriatric Use

In placebo-controlled trials, 42 patients age 60 to 68 years, received doses of 20 mg to 240 mg of fexofenadine twice daily for up to two weeks. Adverse events were similar in this group to patients under age 60 years (Refs. 7,8,46,47).

ADVERSE REACTIONS

In placebo-controlled clinical trials which included 2461 patients receiving fexofenadine hydrochloride at doses of 20 mg to 240 mg twice daily, adverse events were similar in fexofenadine hydrochloride and placebo-treated patients (Refs. 75,78). The incidence of adverse events, including drowsiness, was not dose related and was similar across subgroups defined by age, gender, and race. The percent of patients who withdrew prematurely because of adverse events was 2.2% with fexofenadine hydrochloride vs 3.3% with placebo (Ref. 79,80). All adverse events reported by greater than 1% of patients who received the recommended daily dose of fexofenadine hydrochloride (60 mg twice daily), and that were more common with fexofenadine than placebo, are listed in the following table.

Adverse Experiences Reported in Placebo-Controlled Seasonal Allergic Rhinitis Clinical Trials at Rates of Greater Than 1%

Adverse Experience	*Fexofenadine 60 mg Twice Daily (n=679)*	*Placebo Twice Daily (n=671)*
Viral Infection (cold, flu)	2.5%	1.5%
Nausea	1.6%	1.5%
Dysmenorrhea	1.5%	0.3%
Drowsiness	1.3%	0.9%
Dyspepsia	1.3%	0.6%
Fatigue	1.3%	0.9%

Adverse events occurring in greater than 1% of fexofenadine hydrochloride-treated patients (60 mg twice daily), but that were more common in the placebo-treated group, include headache and throat irritation (Ref. 78).

The frequency and magnitude of laboratory abnormalities were similar in fexofenadine hydrochloride and placebo-treated patients (Ref. 63).

OVERDOSAGE

Information regarding acute overdosage is limited to experience from clinical trials conducted during the development of ALLEGRA™. Single doses of fexofenadine hydrochloride up to 800 mg (6 normal volunteers at this dose level), and doses up to 690 mg twice daily for one month (3 normal volunteers at this dose level), were administered without the development of clinically significant adverse events (Refs. 22,23).

In the event of overdose, consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended.

Hemodialysis did not effectively remove fexofenadine from blood (up to 1.7% removed) following terfenadine administration (Ref. 64).

~~An oral lethal dose in rodents could not be determined for~~ fexofenadine hydrochloride. No deaths occurred at oral doses up to 5000 mg/kg in mice (170 times the maximum recommended human daily oral dose based on mg/m^2) and up to 5000 mg/kg in rats (330 times the maximum recommended human daily oral dose based on mg/m^2 Refs. 65,66). Additionally, no clinical signs of toxicity or gross pathological findings were observed. In dogs, no evidence of toxicity was observed at oral doses up to 2000 mg/kg (450 times the maximum recommended human daily oral dose based on mg/m^2 Refs. 67,68).

DOSAGE AND ADMINISTRATION

The recommended dose of ALLEGRA™ is 60 mg twice daily for adults and children 12 years of age and older (Refs. 7,8).

A dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function. (See CLINICAL PHARMACOLOGY.)

HOW SUPPLIED

ALLEGRA™ 60-mg capsules are available in (Ref. 69): high-density polyethylene (HDPE) bottles of 60 (NDC 0088-1102-41); HDPE bottles of 100 (NDC 0088-1102-47); HDPE bottles of 500 (NDC 0088-1102-55); and aluminum-foil blister packs of 100 (NDC 0088-1102-49).

ALLEGRA™ capsules have a white opaque cap and a pink opaque body. The capsules are imprinted in black ink, with "60 mg" on the cap, and "1102" on the body (Ref. 70).

Store ALLEGRA™ capsules at controlled room temperature 20-25°C (68-77°F) (Ref. 71). Foil-backed blister packs should be protected from excessive moisture (Ref. 81).

Prescribing Information as of July 1996

Hoechst Marion Roussel, Inc.

Kansas City, MO 64137 USA

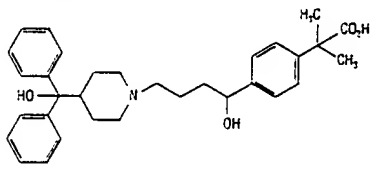
Prescribing Information as of July 1996

ALLEGRA™

(fexofenadine hydrochloride) Capsules 60 mg

DESCRIPTION

Fexofenadine hydrochloride, the active ingredient of ALLEGRA™, is a histamine H_1-receptor antagonist with the chemical name (±)-4-[1-hydroxy-4-[4-(hydroxydiphenylmethyl)-1-piperidinyl]-butyl]-α,α-dimethyl benzeneacetic acid hydrochloride. It has the following chemical structure:



• HCl

The molecular weight is 538.13 and the empirical formula is $C_{32}H_{39}NO_4$•HCl. Fexofenadine hydrochloride is a white to off-white crystalline powder. It is freely soluble in methanol and ethanol, slightly soluble in chloroform and water, and insoluble in hexane. Fexofenadine hydrochloride is a racemate and exists as a zwitterion in aqueous media at physiological pH.

ALLEGRA™ is formulated as capsules for oral administration. Each capsule contains 60 mg fexofenadine hydrochloride and the following excipients: croscarmellose sodium, gelatin, lactose, microcrystalline cellulose, and pregelatinized starch. The printed capsule shell is made from gelatin, iron oxide, silicon dioxide, sodium lauryl sulfate, titanium dioxide, and other ingredients.

CLINICAL PHARMACOLOGY

Mechanism of Action

Fexofenadine, a metabolite of terfenadine, is an antihistamine with selective peripheral H_1-receptor antagonist activity. Fexofenadine inhibited antigen-induced bronchospasm in sensitized guinea pigs and histamine release from peritoneal mast cells in rats. In laboratory animals, no anticholinergic or alpha$_1$-adrenergic-receptor blocking effects were observed. Moreover, no sedative or other central nervous system effects were observed. Radiolabeled tissue distribution studies in rats indicated that fexofenadine does not cross the blood-brain barrier.

Pharmacokinetics

Fexofenadine hydrochloride was rapidly absorbed following oral administration of a single dose of two 60-mg capsules to healthy male volunteers with a mean time to maximum plasma concentration occurring at 2.6 hours postdose. After administration of a single 60-mg dose as an oral solution to healthy subjects, the mean plasma concentration was 209 ng/mL. Mean steady-state peak plasma concentrations of 286 ng/mL were observed when healthy volunteers were administered multiple doses of fexofenadine hydrochloride (60 mg oral solution every 12 hours for 10 doses). Fexofenadine pharmacokinetics were linear for oral doses up to 120 mg twice daily. Although the absolute bioavailability of fexofenadine hydrochloride capsules is unknown, the capsules are bioequivalent to an oral solution. The mean elimination half-life of fexofenadine was 14.4 hours following administration of 60 mg, twice daily, to steady-state in normal volunteers.

Human mass balance studies documented a recovery of approximately 80% and 11% of the [^{14}C] fexofenadine hydrochloride dose in the feces and urine, respectively. Approximately 5% of the total dose was metabolized. Because the absolute bioavailability of fexofenadine hydrochloride has not been established, it is unknown if the fecal component represents unabsorbed drug or the result of biliary excretion.

The pharmacokinetics of fexofenadine hydrochloride in seasonal allergic rhinitis patients were similar to those in healthy subjects. Peak fexofenadine plasma concentrations were similar between adolescent (12-16 years of age) and adult patients.

Fexofenadine is 60% to 70% bound to plasma proteins, primarily albumin and α_1-acid glycoprotein.

Special Populations

Special population pharmacokinetics (for age and renal and hepatic impairment), obtained after a single dose of 60 mg fexofenadine hydrochloride, were compared to those from normal subjects in a separate study of similar design. While subject weights were relatively uniform between studies, these special population patients were substantially older than the healthy, young volunteers. Thus, an age effect may be confounding the pharmacokinetic differences observed in some of the special populations.

Effect of Age. In older subjects (≥65 years old), peak plasma levels of fexofenadine were 99% greater than those observed in normal volunteers (<65 years old). Mean elimination half-lives were similar to those observed in normal volunteers.

Renally Impaired. In patients with mild (creatinine clearance 41-80 mL/min) to severe (creatinine clearance 11-40 mL/min) renal impairment, peak plasma levels of fexofenadine were 87% and 111% greater, respectively, and mean elimination half-lives were 59% and 72% longer, respectively, than observed in normal volunteers. Peak plasma levels in patients on dialysis (creatinine clearance ≤ 10 mL/min) were 82% greater and half-life was 31% longer than observed in normal volunteers. Based on increases in bioavailability and half-life, a dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function. (See DOSAGE AND ADMINISTRATION.)

Hepatically Impaired. The pharmacokinetics of fexofenadine hydrochloride in patients with hepatic disease did not differ substantially from that observed in healthy subjects.

Effect of Gender. Across several trials, no clinically significant gender-related differences were observed in the pharmacokinetics of fexofenadine.

Pharmacodynamics

Wheal and Flare. Human histamine skin wheal and flare studies following single and twice daily doses of 20 mg and 40 mg fexofenadine hydrochloride demonstrated that the drug exhibits an antihistamine effect by 1 hour, achieves maximum effect at 2-3 hours, and an effect is still seen at 12 hours. There was no evidence of tolerance to these effects after 28 days of dosing.

Effects on QTc. In dogs, (10 mg/kg/day, orally for 5 days) and rabbits (10 mg/kg, intravenously over one hour) fexofenadine did not prolong QTc at plasma concentrations that were at least 28 and 63 times, respectively, the therapeutic plasma concentrations in man (based on a 60 mg twice daily fexofenadine hydrochloride dose). No effect was observed on calcium channel current, delayed K^+ channel current, or action potential duration in guinea pig myocytes, Na^+ current in rat neonatal myocytes, or on the delayed rectifier K^+ channel cloned from human heart at concentrations up to 1×10^{-6} M of fexofenadine. This concentration was at least 32 times the therapeutic plasma concentration in man (based on a 60-mg twice daily fexofenadine hydrochloride dose).

No statistically significant increase in mean QTc interval compared to placebo was observed in 714 seasonal allergic rhinitis patients given fexofenadine hydrochloride capsules in doses of 60 mg to 240 mg twice daily for two weeks or in 40 healthy volunteers given fexofenadine hydrochloride as an oral solution at doses up to 400 mg twice daily for 6 days.

Clinical Studies

In three, 2-week, multi-center, randomized, double-blind, placebo-controlled trials in patients 12-68 years of age with seasonal allergic rhinitis (n=1634), fexofenadine hydrochloride 60 mg twice daily significantly reduced total symptom scores (the sum of the individual scores for sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes) compared to placebo. Statistically significant reductions in symptom scores were observed following the first 60-mg dose, with the effect maintained throughout the 12-hour interval. In general, there was no additional reduction in total symptom scores with higher doses of fexofenadine up to 240 mg twice daily. Although the number of subjects in some of the subgroups was small, there were no significant differences in the effect of fexofenadine hydrochloride across subgroups of patients defined by gender, age, and race.

Onset of action for reduction in total symptom scores, excluding nasal congestion, was observed at 50 minutes compared to placebo following a single 60-mg fexofenadine hydrochloride dose administered to patients with seasonal allergic rhinitis who were exposed to ragweed pollen in an environmental exposure unit.

INDICATIONS AND USAGE

ALLEGRA™ is indicated for the relief of symptoms associated with seasonal allergic rhinitis in adults and children 12 years of age and older. Symptoms treated effectively include sneezing, rhinorrhea, itchy nose/palate/throat, itchy/watery/red eyes.

CONTRAINDICATIONS

ALLEGRA™ is contraindicated in patients with known hypersensitivity to any of its ingredients.

PRECAUTIONS

Drug Interactions

In two separate studies, fexofenadine hydrochloride 120 mg twice daily (twice the recommended dose) was co-administered with erythromycin

500 mg every 8 hours or ketoconazole 400 mg once daily under steady-state conditions to normal, healthy volunteers (n=24, each study). No differences in adverse events or QTc interval were observed when subjects were administered fexofenadine hydrochloride alone or in combination with erythromycin or ketoconazole. The findings of these studies are summarized in the following table:

Effects on Steady-State Fexofenadine Pharmacokinetics After 7 Days of Co-Administration with Fexofenadine Hydrochloride 120 mg Every 12 Hours (twice recommended dose) in Normal Volunteers (n=24)

Concomitant Drug	$C_{max,ss}$ *(Peak plasma concentration)*	$AUC_{ss}(0\text{-}12h)$ *(Extent of systemic exposure)*
Erythromycin (500 mg every 8 hrs)	+82%	+109%
Ketoconazole (400 mg once daily)	+135%	+164%

The mechanisms of these interactions are unknown, and the potential for interaction with other azole antifungal or macrolide agents has not been studied. These changes in plasma levels were within the range of plasma levels achieved in adequate and well-controlled clinical trials. Fexofenadine had no effect on the pharmacokinetics of erythromycin or ketoconazole.

Carcinogenesis, Mutagenesis, Impairment of Fertility

The carcinogenic potential and reproductive toxicity of fexofenadine hydrochloride were assessed using terfenadine studies with adequate fexofenadine exposure (based on plasma area-under-the-curve [AUC] values). No evidence of carcinogenicity was observed when mice and rats were given daily oral doses of 50 and 150 mg/kg of terfenadine for 18 and 24 months, respectively; these doses resulted in plasma AUC values of fexofenadine that were up to four times the human therapeutic value (based on a 60-mg twice-daily fexofenadine hydrochloride dose).

In in-vitro (Bacterial Reverse Mutation, CHO/HGPRT Forward Mutation, and Rat Lymphocyte Chromosomal Aberration assays) and in-vivo (Mouse Bone Marrow Micronucleus assay) tests, fexofenadine hydrochloride revealed no evidence of mutagenicity.

In rat fertility studies, dose-related reductions in implants and increases in postimplantation losses were observed at oral doses equal to or greater than 150 mg/kg of terfenadine; these doses produced plasma AUC values of fexofenadine that were equal to or greater than three times the human therapeutic value (based on a 60-mg twice-daily fexofenadine hydrochloride dose).

Pregnancy

Teratogenic Effects: Category C. There was no evidence of teratogenicity in rats or rabbits at oral terfenadine doses up to 300 mg/kg; these doses produced fexofenadine plasma AUC values that were up to 4 and 37 times the human therapeutic value (based on a 60-mg twice-daily fexofenadine hydrochloride dose), respectively.

There are no adequate and well-controlled studies in pregnant women. Fexofenadine hydrochloride should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nonteratogenic Effects. Dose-related decreases in pup weight gain and survival were observed in rats exposed to oral doses equal to and greater than 150 mg/kg of terfenadine; at these doses the plasma AUC values of fexofenadine were equal to or greater than 3 times the human therapeutic values (based on a 60-mg twice-daily fexofenadine hydrochloride dose).

Nursing Mothers

There are no adequate and well-controlled studies in women during lactation. Because many drugs are excreted in human milk, caution should be exercised when fexofenadine hydrochloride is administered to a nursing woman.

Pediatric Use

Safety and effectiveness of ALLEGRA™ in pediatric patients under the age of 12 years have not been established. Across well-controlled clinical trials in patients with seasonal allergic rhinitis, a total of 205 patients between the ages of 12 to 16 years received doses ranging from 20 mg to 240 mg twice daily for up to two weeks. Adverse events were similar in this group compared to patients above the age of 16 years.

Geriatric Use

In placebo-controlled trials, 42 patients, age 60 to 68 years, received doses of 20 mg to 240 mg of fexofenadine twice daily for up to two weeks. Adverse events were similar in this group to patients under age 60 years.

ADVERSE REACTIONS

In placebo-controlled clinical trials, which included 2461 patients receiving fexofenadine hydrochloride at doses of 20 mg to 240 mg twice daily, adverse events were similar in fexofenadine hydrochloride and placebo-treated patients. The incidence of adverse events, including drowsiness, was not dose related and was similar across subgroups defined by age, gender, and race. The percent of patients who withdrew prematurely because of adverse events was 2.2% with fexofenadine hydrochloride vs 3.3% with placebo. All adverse events that were reported by greater than 1% of patients who received the recommended daily dose of fexofenadine hydrochloride (60 mg twice-daily), and that were more common with fexofenadine than placebo, are listed in the following table.

Adverse Experiences Reported in Placebo-Controlled Seasonal Allergic Rhinitis Clinical Trials at Rates of Greater Than 1%

Adverse Experience	*Fexofenadine 60 mg Twice Daily (n=679)*	*Placebo Twice Daily (n=671)*
Viral Infection (cold, flu)	2.5%	1.5%
Nausea	1.6%	1.5%
Dysmenorrhea	1.5%	0.3%
Drowsiness	1.3%	0.9%
Dyspepsia	1.3%	0.6%
Fatigue	1.3%	0.9%

Adverse events occurring in greater than 1% of fexofenadine hydrochloride-treated patients (60 mg twice daily), but that were more common in the placebo-treated group, include headache and throat irritation.

The frequency and magnitude of laboratory abnormalities were similar in fexofenadine hydrochloride and placebo-treated patients.

OVERDOSAGE

Information regarding acute overdosage is limited to experience from clinical trials conducted during the development of ALLEGRA™. Single doses of fexofenadine hydrochloride up to 800 mg (6 normal volunteers at this dose level), and doses up to 690 mg twice daily for one month (3 normal volunteers at this dose level), were administered without the development of clinically significant adverse events.

In the event of overdose, consider standard measures to remove any unabsorbed drug. Symptomatic and supportive treatment is recommended.

Hemodialysis did not effectively remove fexofenadine from blood (up to 1.7% removed) following terfenadine administration.

No deaths occurred at oral doses of fexofenadine hydrochloride up to 5000 mg/kg in mice (170 times the maximum recommended human daily oral dose based on mg/m^2) and up to 5000 mg/kg in rats (330 times the maximum recommended human daily oral dose based on mg/m^2). Additionally, no clinical signs of toxicity or gross pathological findings were observed. In dogs, no evidence of toxicity was observed at oral doses up to 2000 mg/kg (450 times the maximum recommended human daily oral dose based on mg/m^2).

DOSAGE AND ADMINISTRATION

The recommended dose of ALLEGRA™ is 60 mg twice daily for adults and children 12 years of age and older.

A dose of 60 mg once daily is recommended as the starting dose in patients with decreased renal function. (See CLINICAL PHARMACOLOGY.)

HOW SUPPLIED

ALLEGRA™ 60-mg capsules are available in: high-density polyethylene (HDPE) bottles of 60 (NDC 0088-1102-41); HDPE bottles of 100 (NDC 0088-1102-47); HDPE bottles of 500 (NDC 0088-1102-55); and aluminum-foil blister packs of 100 (NDC 0088-1102-49).

ALLEGRA™ capsules have a white opaque cap and a pink opaque body. The capsules are imprinted in black ink, with "60 mg" on the cap, and "1102" on the body.

Store ALLEGRA™ capsules at controlled room temperature 20-25°C (68-77°F). Foil-backed blister packs should be protected from excessive moisture.

Prescribing information as of July 1996

Hoechst Marion Roussel, Inc.
Kansas City, MO 64137 USA

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Carr et al.

[11] 4,254,129

[45] Mar. 3, 1981

[54] PIPERIDINE DERIVATIVES

[75] Inventors: Albert A. Carr; Joseph E. Dolfini, both of Cincinnati, Ohio; George J. Wright, Richmond, Va.

[73] Assignee: Richardson-Merrell Inc., Wilton, Conn.

[21] Appl. No.: 28,813

[22] Filed: Apr. 10, 1979

[51] Int. Cl.³ C07D 211/34; A61K 31/445

[52] U.S. Cl. 424/267; 546/239; 546/240

[58] Field of Search 546/239, 240; 424/267

[56] References Cited

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3,687,956	8/1972	Zivkovic	546/240
3,806,526	4/1974	Carr et al.	546/237
3,829,433	8/1974	Carr et al.	546/237
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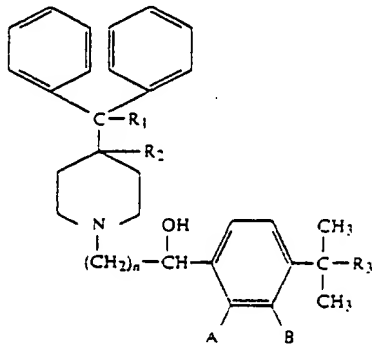
3,965,257	6/1976	Carr et al.	546/237

Primary Examiner—Norma S. Milestone

Attorney, Agent, or Firm—John J. Kolano; George W. Rauchfuss, Jr.; Salvatore R. Conte

[57] ABSTRACT

Novel compounds of the following formula:



wherein R_1 is hydrogen or hydroxy; R_2 is hydrogen; or R_1 and R_2 taken together form a second bond between the carbon atoms bearing R_1 and R_2; n is an integer of from 1 to 5; R_3 is $-CH_3$, $-CH_2OH$, —COOH or —COOalkyl wherein the alkyl moiety has from 1 to 6 carbon atoms and is straight or branched; and each of A and B is hydrogen or hydroxy; with the provisos that at least one of A or B is hydrogen and one of A or B is other than hydrogen when R_3 is $-CH_3$; and pharmaceutically acceptable salts thereof.

11 Claims, No Drawings

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

F

Food and Drug Administration
Rockville MD 20857

IND 43,573

Date October 7, 1993

Marion Merrell Dow, Inc.
Marion Park Drive
Kansas City, MO 64134

Attn: Elaine Waller, PharmD
Vice President
US Regulatory Affairs

Dear Sir or Madam:

We acknowledge receipt of your Investigational New Drug Application (IND) submitted pursuant to Section 505(i) of the Federal Food, Drug, and Cosmetic Act. Please note the following identifying data:

IND Number Assigned: 43,573

Sponsor: Marion Merrell Dow, Inc.

Name of Drug: MDL 16,455A

Date of Submission: October 4, 1993

Date of Receipt: October 5, 1993

Studies in humans may not be initiated until 30 days after the date of receipt shown above. If, within the 30-day waiting period, we identify deficiencies in the IND that require correction before human studies begin or that require restriction of human studies until correction, we will notify you immediately that the study may not be initiated ("clinical hold") or that certain restrictions must be placed on it. In the event of such notification, you must continue to withhold, or to restrict, such studies until you have submitted material to correct the deficiencies, and we have notified you that the material you submitted is satisfactory.

It has not been our policy to object to a sponsor, upon receipt of this acknowledgement letter, either obtaining supplies of the investigational drug or shipping it to investigators listed in the IND. However, if drug is shipped to investigators, they should be reminded that studies may not begin under the IND until 30 days after the IND receipt date or later if the IND is placed on clinical hold.

FOCUS:43,573:931007

bcc: EWaller, BDavidson, JHemberger, JKeyser, KWhite, MNicholas, EMitchell, GIvers-Read, MQuigley, CKirk-Yourtee, LStewart, DEmerson, PAdams, SHotchkiss, MShoemaker, BGuiffy

FORM FDA 2238 (4/89) PREVIOUS EDITIONS OBSOLETE.

You are responsible for compliance with the Federal Food, Drug, and Cosmetic Act and the regulations implementing that Act (Title 21 of the Code of Federal Regulations). Those responsibilities include reporting any adverse experience associated with use of the drug that is both serious and unexpected to the FDA as soon as possible and in no event later than 10 working days after initial receipt of the information and reporting any unexpected fatal or life-threatening experience to the FDA by telephone no later than 3 working days after receipt of the information (21 CFR 312.32), and submission of annual progress reports (21 CFR 312.33).

Please forward all future communications concerning this IND in triplicate, identified by the above IND number, and addressed as follows:

Food and Drug Administration
Center for Drug Evaluation and Research (HFD- 155)
Attention: Document Control Room
5600 Fishers Lane
Rockville, Maryland 20857

Should you have any questions concerning this IND, please contact Mr. Conrad Ledet at (301) 443-~~4260~~ 4260

Sincerely yours,

Conrad J. Ledet

Center for Drug Evaluation and Research

cc: Original IND - pink
HFD-155 - yellow
HFD-155/CSO - green

IND ACKNOWLEDGEMENT

MARION MERRELL DOW INC.

Marion Park Drive
MAIL: P.O. Box 9627
Kansas City, Missouri 64134-0627
Telephone: 816/966-5000

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July 31, 1995

Food and Drug Administration
Office of Drug Evaluation and Research
Central Document Room
Park Building, Room 214
1240 ParkLawn Drive
Rockville, MD 20852

Subject: New Drug Application
Fexofenadine HCl Capsules
(MDL 16,455A)
NDA 20-625

Dear Madames/Messiers:

In conformance with 21 CFR 314.1, Hoechst Marion Roussel, Inc. is submitting a New Drug Application (NDA) for fexofenadine HCl, 60 mg capsules. This NDA provides support for the use of fexofenadine HCl in the relief of symptoms associated with seasonal allergic rhinitis. The proposed dosage regimen for seasonal allergic rhinitis patients is 60 mg BID. The submission is 454 volumes in length. Contents of the submission include the following sections:

1) Index
2) Application Summary
3) Chemistry, Manufacturing and Control
4) Methods, Validation and Labeling
5) Nonclinical Pharmacology and Toxicology
6) Human Pharmacokinetics and Bioavailability
8) Clinical Data
10) Statistical Section
11) Case Report Tabulations
12) Case Report Forms
13/14) Patent Information and Certification

This submission is paginated to reflect the Section number (S), followed by Volume number (V), and by Page (P). A separate identical copy of Section 3. Chemistry, Manufacturing and Control has been issued to the local District Office.

Fexofenadine HCl development has been a product of collaborative efforts between the sponsor and Reviewing Division of the FDA. The free-base of fexofenadine HCl or MDL 16,455A (MDL 16,455) was identified as an active acid metabolite of terfenadine. Terfenadine has been marketed globally for over a decade for use in symptomatic relief of seasonal allergic rhinitis and is currently marketed in over 150 countries. While terfenadine has proven to be safe and effective when used under prescribed conditions elevated levels of terfenadine, whether due to hepatic dysfunction, concomitant medications or overdose.

have been associated with QTc interval prolongation. The acid metabolite of terfenadine, fexofenadine HCl, was found to exhibit antihistaminic properties without adverse cardiovascular side effects as observed in animal studies. As a result, Hoechst Marion Roussel, Inc. initiated clinical studies to determine safety and efficacy of the drug product in humans.

This NDA provides data to support the safety and efficacy of fexofenadine HCl (MDL 16,455A) in relief of symptoms of seasonal allergic rhinitis. Four adequate and well controlled clinical studies were conducted with fexofenadine HCl. All four studies were multicenter, randomized, double-blind, placebo-controlled, dose-response studies in patients with seasonal allergic rhinitis (SAR). Two studies were conducted in the spring (Protocol PJPR0009 and PJPR0010) and two studies were conducted in the fall (Protocols PJPR0023 and PJPR0024). Protocols PJPR0009 (962 intent-to-treat patients), PJPR0010 (995 intent-to-treat patients), PJPR0023 (570 intent-to-treat patients) and PJPR0024 (545 intent-to-treat patients) demonstrate effectiveness of fexofenadine HCl at doses ranging from 40 mg BID to 240 mg BID, in the treatment of the symptomatic relief of seasonal allergic rhinitis during both spring and fall seasons. Fexofenadine HCl reduced severity of individual symptoms (sneezing, rhinorrhea, itchy nose, palate and/or throat; and itchy, watery, red eyes) as well as total symptom scores. In addition, a study conducted to assess onset of action (PJPR0017) demonstrated effect one hour following a single dose of 60 mg. Analysis of the four adequate and well controlled studies shows the 60 mg dose had a faster onset of action than the 40 mg dose. Similar onset of effect was observed for doses of 60 mg to 240 mg BID of fexofenadine.

Under conditions of use defined in the proposed text of labeling, benefits of fexofenadine HCl 60 mg BID use in the relief of symptoms of seasonal allergic rhinitis outweigh any anticipated risk.

We look forward to your review of our New Drug Application for fexofenadine HCl. Please be advised that the information submitted is considered confidential under 21 CFR 314.430.

If you have any questions, please do not hesitate to contact:

Dr. Cynthia Kirk-Yourtee
Hoechst Marion Roussel, Inc.
P.O. Box 9707, Park A1
Kansas City, MO 64134-0707
(816) 966-5076

Sincerely,

Elaine Waller

Elaine Waller, PharmD
Vice President,
U.S. Regulatory Affairs

8.D. Controlled Clinical Trials
1. Table of All Controlled Studies

D. Controlled Clinical Trials

1. Table of All Controlled Studies

Guide to Abbreviations and Footnotes		
PLAC	=	Placebo
AEs	=	Adverse Events
PE	=	Physical Exam
M:F	=	Male: Female
PG/AA	=	1.5% glacial acetic acid/98.5% propylene glyocol (v/v)
SAR	=	Seasonal Allergic Rhinitis
DBPC	=	Double-Blind Placebo Controlled
Clin Lab	=	Clinical Laboratory
Wks	=	Weeks
1°	=	Primary
ECG	=	Electrocardiogram
CRFs	=	Case Report Forms
Vol	=	Volume
PK	=	Pharmacokinetics

Table 8–240. Table of All Controlled Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Data Listings/ CRFs					
PJPR0009 Investigators (see listing below) Amendment 1: 3/1/94 Amendment 2: 4/14/94 Amendment 3: 5/9/94 Amendment 4: 6/16/94 Report: K-94-0780-CDS Tabulations: K-94-0781-S	Complete (3/2/94 to 7/15/94)	US. MDL 16,455A Gelatin Capsules 20 mg	Full Report: *S8–V1.185–P12* Tabulations: *S11–V1.312–P21* CRFs: *S12–V1.447–P3*	DBPC, randomized, parallel, multiple dose, multicenter 1° Efficacy: • Symptom assessments Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals PK: • Plasma samples	Multiple dose PLAC Q12h: 193 20 mg Q12h: 195 40 mg Q12h: 196 60 mg Q12h: 197 80 mg Q12h: 194 Screened: 1194 Randomized: 982 Exposed to DB Treatment: 975 Safety Eval: 972 Completed: 919 Early DC: 56	782	Population: SAR patients Gender: M:F 415:560 Race: * Caucasian 861 Black 86 Asian 26 Other 2 Age: Range: 11-65 Mean ± SD 32 ± 11	Single-blind PLAC Lead-in: 2 days Double-blind PLAC or MDL 16,455A: 2 wks

* Values for race may differ from the individual CSR because RACE was classified into standard categories for the Integrated Database for the ISS.

Study Site	Investigator	No. Exposed	Study Site	Investigator	No. Exposed
PJST0014	Jeffrey M Adelglass, MD	70	PJST0022	Bruce M Prenner, MD	59
PJST0015	David I Bernstein, MD	55	PJST0023	James P Rosen, MD	58
PJST0016	Edwin A Bronsky, MD	59	PJST0024	James M Seltzer, MD	70
PJST0017	B Lauren Charous, MD	59	PJST0025	Chester T Stafford, MD	69
PJST0018	Donald J Dvorin, MD	60	PJST0026	James E Stroh, MD	59
PJST0019	Constantine J Falliers, MD	70	PJST0027	Julius H van Bavel, MD	69
PJST0020	John W Georgitis, MD	60	PJST0028	Jeffrey A Wald, MD	60
PJST0021	Frank C Hampel, Jr, MD	70	PJST0029	Martha V White, MD	28

Table 8-240. Table of All Controlled Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Data Listings/ CRFs					
PJPR0010 Investigators (see listing below) Amendment 1: 3/1/94 Amendment 2: 4/14/94 Amendment 3: 5/9/94 Amendment 4: 6/16/94 Report: K-94-0782-CDS Tabulations: K-94-0783-S	Complete (3/17/94 to 7/19/94)	US MDL 16,455A Gelatin Capsules 20 mg	Full Report: *S8–V1.202–P1* Tabulations: *S11–V1.336–P1* CRFs: *S12–V1.449–P1*	DBPC, randomized, parallel, multiple dose, multicenter 1° Efficacy: • Symptom assessments Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals PK: • Plasma samples	Multiple dose PLAC Q12h: 202 20 mg Q12h: 199 40 mg Q12h: 203 60 mg Q12h: 205 80 mg Q12h: 202 Screened: 1203 Randomized: 1021 Exposed to DB Treatment: 1011 Safety Eval: 1004 Completed: 942 Early DC: 70	809	Population: SAR patients Gender: M:F 462:549 Race: * Caucasian 882 Black 73 Asian 56 Age: Range: 12-68 Mean ± SD 33 ± 12	Single-blind PLAC Lead-In: 2 days Double-blind PLAC or MDL 16,455A: 2 wks

* Values for race may differ from the individual CSR because RACE was classified into standard categories for the Integrated Database for the ISS.

Study Site	Investigator	No. Exposed	Study Site	Investigator	No. Exposed
PJST0030	Paul Chervinsky, MD	60	PJST0038	David S Pearlman, MD	70
PJST0031	Theodore J Chu, MD	60	PJST0039	Gordon D Raphael, MD	70
PJST0032	Robert J Dockhorn, MD	60	PJST0040	Paul H Rainer, MD	77
PJST0033	Thomas B Edwards, MD	60	PJST0041	Allen T Segal, MD	70
PJST0034	Jay Grossman, MD	67	PJST0042	Sheldon L Spector, MD	57
PJST0035	William C Howland, III, MD	59	PJST0043	David G Tinkelman, MD	60
PJST0036	Harold B Kaiser, MD	65	PJST0044	John A Winder, MD	59
PJST0037	Eli O Meltzer, MD	59	PJST0045	Thomas R Woehler, MD	59

Table 8–240. Table of All Controlled Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Data Listings/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0023 Investigators (see listing below) Amendment 1: 8/3/94 Amendment 2: 8/25/94 Amendment 3: 9/23/94 Amendment 4: 9/23/94 Amendment 5: 11/15/94 Report: K-95-0005-CDS Tabulations: K-95-0006-S	Complete (8/15/94 to 11/19/94)	US MDL 16,455A Gelatin Capsules 60 mg (Full scale)	Full Report: *S8–V1.219–P1* Tabulations: *S11–V1.361–P1* CRFs: *S12–V1.452–P1*	DBPC, randomized, parallel, multiple dose, multicenter 1° Efficacy: • Symptom assessments Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Plasma samples	Multiple dose PLAC Q12h: 142 60 mg Q12h: 141 120 mg Q12h: 144 240 mg Q12h: 145 Screened: 1498 Entered: 1073 Randomized: 575 Exposed to DB Treatment: 572 Safety Eval: 572 Completed: 544 Early DC: 28	430	Population: SAR patients Gender: M:F 237:335 Race:* Caucasian 535 Black 35 Asian 2 Age: Range: 12-66 Mean ± SD 33 ± 11	Single-blind PLAC Lead-in: 3 days Double-blind PLAC or MDL 16,455A: 2 wks

* Values for race may differ from the individual CSR because RACE was classified into standard categories for the Integrated Database for the ISS.

Study Site	Investigator	No. Exposed	Study Site	Investigator	No. Exposed
016455ST0134	Jeffrey M Adelglass, MD	37	016455ST0143	John A Holmes, MD	25
016455ST0135	Charles H Banov, MD	50		Anthony J Silvagni, DO	
016455ST0136	David I Bernstein, MD	33	016455ST0144	Robert A Nathan, MD	15
016455ST0137	Peter B Boggs, MD	64	016455ST0145	Gordon D Raphael, MD	37
016455ST0138	B Lauren Charous, MD	15	016455ST0146	James P Rosen, MD	32
016455ST0139	Robert J Dockhorn, MD	30		Jeffrey M Factor, MD	
016455ST0140	John W Georgitis, MD	32	016455ST0147	Wm F Schoenwetter, MD	43
016455ST0141	Jay Grossman, MD	50	016455ST0148	Julius H van Bavel, MD	40
016455ST0142	Frank C Hampel, Jr, MD	57	016455ST0169	Robert M Cohen, MD	12

Table 8–240. Table of All Controlled Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Data Listings/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0024 Investigators (see listing below) Amendment 1: 8/3/94 Amendment 2: 8/25/94 Amendment 3: 9/23/94 Amendment 4: 9/23/94 Amendment 5: 11/15/94 Report: K-95-0007-CDS Tabulations: K-95-0008-S	Complete (8/12/94 to 11/30/94)	US MDL 16,455A Gelatin Capsules 20 mg (Pilot scale) and 40 mg (Full scale)	Full Report: *S8–V1.239–P1* Tabulations: *S11–V1.381–P1* CRFs: *S12–V1.454–P1*	DBPC, randomized, parallel, multiple dose, multicenter 1° Efficacy: • Symptom assessments Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Plasma samples	Multiple dose PLAC Q12h: 148 40 mg Q12h: 145 60 mg Q12h: 148 120 mg Q12h: 147 Screened: 1345 Entered: 1046 Randomized: 589 Exposed to DB Treatment: 588 Safety Eval: 588 Completed: 550 Early DC: 38	440	Population: SAR patients Gender: M:F 229:359 Race: * Caucasian 534 Black 41 Asian 11 Other 2 Age: Range: 12-63 Mean ± SD 33 ± 11	Single-blind PLAC Lead-in: 3 days Double-blind PLAC or MDL 16,455A: 2 wks

* Values for race may differ from the individual CSR because RACE was classified into standard categories for the Integrated Database for the ISS.

Study Site	Investigator	No. Exposed	Study Site	Investigator	No. Exposed
016455ST0149	Edwin A Bronsky, MD David L Goodman, MD	41	016455ST0157	James H Ransom, MD	42
016455ST0150	Donald J Dvorin, MD	47	016455ST0158	Paul H Ratner, MD	39
016455ST0151	Thomas B Edwards, MD	30	016455ST0159	Allen T Segal, MD	23
016455ST0152	Constantine J Falliers, MD	48	016455ST0160	David G Tinkelman, MD	48
016455ST0153	William C Howland, III, MD	39	016455ST0161	Jeffrey A Wald, MD	16
016455ST0154	Harold B Kaiser, MD	56	016455ST0162	Allan M Weinstein, MD Richard J Summers, MD	12
016455ST0155	Craig F LaForce, MD	39	016455ST0163	John A Winder, MD	23
016455ST0156	Zev M Munk, MD	40	016455ST0167	Nabeeh N LaHood, MD	45

Table 8–240. Table of All Controlled Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Data Listings/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0014 Investigators (see listing below) Report: K-95-0054-CS Tabulations: K-95-0055-S	Complete (6/13/94 to 9/30/94)	US MDL 16,455A Gelatin Capsules 20 mg	Full Report: *S8–V1.259–P2* Tabulations: *S11–V1.402–P1* CRFs: None	DBPC, randomized, parallel, safety tolerance, multiple dose, multicenter Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG	Multiple dose PLAC Q12h: 14 80 mg Q12h: 27 Screened: 80 Randomized: 41 Exposed to DB Treatment: 41 Safety Eval: 40 Completed: 40 Early DC: 1	27	Population: Healthy subjects Gender: M:F 16:25 Race: Caucasian 38 Black 3 Age: Range: 12-56 Mean ± SD 32 ± 12	Double-blind PLAC or MDL 16,455A: 3 months

Study Site	Investigator	No. Entered	Study Site	Investigator	No. Entered
PJST0048	David I Bernstein, MD	0	PJST0056	James E Stroh, MD	0
PJST0049	Robert J Dockhorn, MD	0	PJST0057	Jeffrey A Wald, MD	7
PJST0050	Frank C Hampel, Jr, MD	20			
PJST0051	Eli O Meltzer, MD	0			
PJST0052	Bruce M Prenner, MD	1			
PJST0053	Gordon D Raphael, MD	12			
PJST0054	Paul H Ratner, MD	1			
PJST0055	James P Rosen, MD	0			

Table 8–240. Table of All Controlled Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Data Listings/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
016455PR0027 (PJPR0027) Investigators (see listing below) Amendment 1: 3/13/95	Ongoing	US MDL 16,455A Gelatin Capsules 60 mg	Full Report: N/A Tabulations: N/A CRFs: N/A	DBPC, randomized, parallel, multiple dose, multicenter Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECGs PK: • Plasma samples	PLAC or 240 mg Q24h	Planned: 400	Population: Healthy subjects	Double-blind PLAC or MDL16,455A: 1 year

Study Site	Investigator	No. Entered	Study Site	Investigator	No. Entered
016455ST0194	Albert F Finn, Jr, MD	30	016455ST0202	Zev M Munk, MD	28
016455ST0195	Peter B Boggs, MD	8	016455ST0203	Robert A Nathan, MD	32
016455ST0196	Robert M Cohen, MD	32	016455ST0204	Scott L Osur, MD	36
016455ST0197	Constantine J Falliers, MD	32	016455ST0205	Allen T Segal, MD	31
016455ST0198	Jay Grossman, MD	18	016455ST0206	James M Seltzer, MD	36
016455ST0199	William C Howland, III, MD	40	016455ST0207	David G Tinkelman, MD	36
016455ST0200	Harold B Kaiser, MD	31			
016455ST0201	Dennis N Morrison, DO	75			

Table 8–240. Table of All Controlled Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Data Listings/ CRFs					
016455PR0031 (PJPR0031) Investigators (see listing below) Amendment 1: 3/13/95	Ongoing	US MDL 16,455A Gelatin Capsules 60 mg	Full Report: N/A Tabulations: N/A CRFs: N/A	DBPC, randomized, parallel, multiple dose, multicenter Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECGs PK: • Plasma samples	PLAC or 60 mg Q12h	Planned: 400	Population: Healthy subjects	Double-blind PLAC or MDL16,455A: 6 months

Study Site	Investigator	No. Entered	Study Site	Investigator	No. Entered
016455ST0179	Jeffrey M Adelglass, MD	30	016455ST0186	Eli O Meltzer, MD	32
016455ST0180	David I Bernstein, MD	30		Nancy K Ostrom, MD	
016455ST0181	Edwin A Bronsky, MD	29	016455ST0187	Bruce M Prenner, MD	32
	David Goodman, MD		016455ST0188	Gordon D Raphael, MD	24
016455ST0182	Robert J Dockhorn, MD	30	016455ST0189	Paul H Ratner, MD	30
016455ST0183	Donald J Dvorin, MD	15	016455ST0190	James P Rosen, MD	29
016455ST0184	Stanley P Galant, MD	28	016455ST0191	Nathan Segall, MD	30
	William G Harris, MD		016455ST0192	James E Stroh, MD	29
016455ST0185	Frank C Hampel, MD	29	016455ST0193	Jeffrey A Wald, MD	30

Table 8–240. Table of All Controlled Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Data Listings/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
016455PR0032 (PJPR0032) Investigators (see listing below)	Ongoing	UK, France, Belgium, Germany MDL 16,455A Gelatin Capsules 60 mg Cetirizine 10 mg	Full Report: N/A Tabulations: N/A CRFs: N/A	DBPC, randomized, parallel, multiple dose, multicenter 1° Efficacy • Symptom assessments Safety: • Treatment-emergent AEs • PE, Clin lab, Vitals	PLAC, 120 or 180 mg daily Cetirizine 10 mg daily	Planned: 400	Population: SAR patients	Single-blind PLAC Lead-in: 5 days Double-blind PLAC, MDL 16,455A, or cetirizine: 2 wks

Study Site	*Investigator	No. Entered	Study Site	*Investigator	No. Entered
016455ST0223	Bousquet, MD		016455ST0237	Metayer, MD	
016455ST0225	Bessot, MD		016455ST0238	Navarro, MD	
016455ST0226	Beutler, MD		016455ST0239	Perrin-Fayolle, MD	
016455ST0227	Carre-Faure, MD		016455ST0240	Piperno, MD	
016455ST0228	F Chabolle, MD		016455ST0241	Rochemaure, MD	
016455ST0229	Clardelli, MD		016455ST0242	Sabbah, MD	
016455ST0231	Favennec, MD		016455ST0243	Severac, MD	
016455ST0232	Cormary, MD		016455ST0244	Waguet, MD	
016455ST0233	Grosclaude, MD		016455ST0245	Wessel, MD	
016455ST0234	Guinnepain, MD		016455ST0260	Barrage, MD	
016455ST0235	Jung, MD		016455ST0261	Delaval, MD	
016455ST0236	F Leynadier, MD				

* Note: This list of investigators is incomplete since all investigators had not been identified at the time of submission.

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location* — *Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
Bioavailability, Bioequivalence, Food Effect								
PJPR0001 SD Oliver, MD Amendment 1: 7/13/93 Report: K-95-0061-DS Tabulations: K-95-0062-S	Complete (8/23/93 to 12/6/93)	UK Treatment A: MDL 16,455A Micellular Soln 6 mg/mL Treatment B: MDL 16,455A 30 mg Uncoated Tablets (Pilot scale) Treatment C: MDL 16,455A PG/AA Soln 22.5 mg/mL	Full Report: *S6–V1.22–P2* Tabulations: *S11–V1.403–P2* CRFs: *S12–V1.444–P6*	Open, randomized, 3-way Xover, single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood & urine sampling	Treatment A: 90 mg single dose: 23 Treatment B: 90 mg single dose: 24 Treatment C: 90 mg single dose: 23 Early DC: 1	24	Population: Healthy subjects Gender: M:F 24:0 Race: Caucasian 23 Black 1 Age: Range: 18-46 Mean ± SD 26 ± 7	Treatment A: Single dose Treatment B: Single dose Treatment C: Single dose 7 day washout between treatments

fexofenadine hydrochloride capsule

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
P.JPR0005 SD Oliver, MD Report: K 95-0050-DS Tabulations: K-95 0051-S	Complete (10/8/93 to 10/27/93)	UK Treatment A: MDL 16,455A Uncoated Tablets 30 mg (Pilot scale) Treatment B: MDL 16,455A Gelatin Capsules 30 mg (Pilot scale) Treatment C: MDL 16,455A PG/AA Soln 22.5 mg/mL	Full Report: *S6-V1.25-P1* Tabulations: *S11-V1.404-P1* CRFs: *S12-V1.444-P93*	Open, randomized, 3-way Xover, single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood & urine sampling	Treatment A: 90 mg single dose: 23 Treatment B: 90 mg single dose: 24 Treatment C: 90 mg single dose: 24 Early DC: 1	24	Population: Healthy subjects Gender: M:F 24:0 Race: Caucasian 24 Age: Range: 19-40 Mean ± SD 26 ± 6	Treatment A: Single dose Treatment B: Single dose Treatment C: Single dose 7 day washout period between treatments

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Tabulations/ CRFs					
PJPR0012 JC Kisicki, MD Report: K-94-0768-DS Tabulations: K-94-0769-S	Complete (1/22/94 to 2/21/94)	US Treatment A: MDL 16,455A PG/AA Soln 20 mg/mL after fasting Treatment B: MDL 16,455A 20 mg Gelatin Capsules after fasting (Pilot scale) Treatment C: MDL 16,455A 20 mg Gelatin Capsules after high fat breakfast (Pilot scale)	Full Report: *S6-V1.28-P1* Tabulations: *S11-V1.405-P1* CRFs: None	Open, randomized, 5 period Xover, single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood and urine sampling	Treatment A: 80 mg single dose: 24 Treatment B: 80 mg single dose: 24 Treatment C: 80 mg single dose: 24 Early DC: 0	24	Population: Healthy subjects Gender: M:F 24:0 Race: Caucasian 23 Black 1 Age: Range: 19-45 Mean ± SD 26 ± 6	Treatment A: Single dose, X2 Treatment B: Single dose, X2 Treatment C: Single dose 7 day washout period between treatments

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0015 JC Kisicki, MD Report: K-94-0742-CDS Tabulations: K-94-0743-S	Complete (4/30/94 to 5/31/94)	US Treatment A: MDL 16,455A PG/AA Soln 22.5 mg/mL Treatment B: MDL 16,455A 30 mg Gelatin Capsules (Pilot scale) Treatment C: MDL 16,455A 30 mg Tablets + Mg Stearate (Pilot scale) Treatment D: MDL 16,455A 30 mg Milled Drug Tablets (Pilot scale)	Full Report: *S6-V1.30-P1* Tabulations: *S11-V1.406-P1* CRFs: None	Open, randomized, 4-way Xover, single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals PK: • Serial blood sampling	Treatment A: 90 mg single dose: 20 Treatment B: 90 mg single dose: 20 Treatment C: 90 mg single dose: 20 Treatment D: 90 mg single dose: 20 Treatment E: 90 mg single dose: 19 Treatment F: 90 mg single dose: 19 Early DC: 0	30	Population: Healthy subjects Gender: M:F 30:0 Race: Caucasian 29 Black 1 Age: Range: 19-45 Mean ± SD 28 ± 7	Treatment A: Single dose Treatment B: Single dose Treatment C: Single dose Treatment D: Single dose Treatment E: Single dose Treatment F: Single dose 7-14 day washout period between treatments

fexofenadine hydrochloride capsule

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0015 (cont)		Treatment E: MDL 16,455A 30 mg Milled Drug + Gelatin Tablets (Pilot scale) Treatment F: MDL 16,455A 30 mg Gelatin Capsules + Mg Stearate (Pilot scale)						
PJPR0025 RJ Dockhorn, MD Amendment 1: 9/26/94 Report: K-95-0034-DS Tabulations: K-95-0035-S	Complete (9/23/94 to 11/3/94)	US Treatment A: MDL 16,455A Gelatin Capsules 60 mg (Full scale) Treatment B: MDL 16,455A Gelatin Capsules 20 mg (Pilot scale) Treatment C: MDL 16,455A PG/AA Soln 30 mg/mL	Full Report: *S6-V1.32-P1* Tabulations: *S11-V1.407-P1* CRFs: None	Open, randomized, repeated treatment, 5-way Xover, single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood sampling	Treatment A: 120 mg single dose: 21 Treatment B: 120 mg single dose: 23 Treatment C: 120 mg single dose: 22 Early DC: 3	24	Population: Healthy subjects Gender: M:F 24:0 Race: Caucasian 18 Black 4 Asian 2 Age: Range: 19-43 Mean ± SD 28 ± 7	Treatment A: Single dose, X2 Treatment B: Single dose, X2 Treatment C: Single dose 7 day washout period between treatments

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
P.JPR0026 D Morrison, DO Amendment 1: 10/27/94 Interim Report: K-95-0109-DS Tabulations: K-95-0110-S	Complete (11/12/94 to 12/19/94)	US Treatment A: MDL 16,455A Gelatin Capsules 40 mg after fasting (Full scale) Treatment B: MDL 16,455A Gelatin Capsules 40 mg after high fat breakfast (Full scale) Treatment C: MDL 16,455A Experimental Gelatin Capsules 40 mg fasted	Full Report: *S6–V1.35–P1* Tabulations: *S11–V1.408–P1* CRFs: None	Open, randomized, 5-way Xover, single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood & urine sampling	Treatment A: 80 mg single dose: 24 Treatment B: 80 mg single dose: 24 Treatment C: 80 mg single dose: 25 Treatment D: 80 mg single dose: 24 Treatment E: 80 mg single dose: 24 Early DC: 1	25	Population: Healthy subjects Gender: M:F 25:0 Race: Caucasian 24 Black 1 Age: Range: 18-41 Mean ± SD 25 ± 6	Treatment A: Single dose Treatment B: Single dose Treatment C: Single dose Treatment D: Single dose Treatment E: Single dose 6 day washout between treatments

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Tabulations/ CRFs					
PJPR0026 (cont)		Treatment D: MDL 16,455A Experimental Gelatin Capsules 40 mg fasted Treatment E: MDL 16,455A Experimental Gelatin Capsules 40 mg fasted						

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	Status (Start Date/ Completion Date)	Study Location, Formulation	NDA Data Location: Full Report/ Tabulations/ CRFs	Study Design	Doses, No. Entered Each Treatment	Total Exposed to MDL 16,455A	Demographics	Duration of Drug Treatment
P.JPR0029 RJ Dockhorn, MD Report: K 95 0165-DS Tabulations: K 95 0166-S	Complete (12/27/94 to 2/8/95)	US Treatment A: MDL 16,455A Gelatin Capsules 40 mg after fasting (Full scale) Treatment B: MDL 16,455A Coated Tablets 40 mg + Mg Stearate after fasting (Full scale) Treatment C: MDL 16,455A Gelatin Capsules 40 mg after high fat breakfast	Full Report: S6–V1.37–P1 Tabulations: S11–V1.409–P1 CRFs: None	Open, randomized, repealed treatment, 5-way Xover, single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood sampling	Treatment A: 120 mg single dose: 23 Treatment B: 120 mg single dose: 23 Treatment C: 120 mg single dose: 24 Early DC: 2	24	Population: Healthy subjects Gender: M:F 24:0 Race: Caucasian 19 Black 5 Age: Range: 20-43 Mean ± SD 28 ± 7	Treatment A: Single dose, X2 Treatment B: Single dose, X2 Treatment C: Single dose 6 day washout period between treatments

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
Mass Balance/Metabolism								
PJPR0008 JC Kisicki, MD Amendment 1: 10/14/93 Report: K-94-0833-DS Tabulations: K-94-0834-S	Complete (12/1/93 to 12/17/93)	US MDL 16,455A PG/AA Soln 15 mg/mL [14C] MDL 16,455A in PG/AA Soln 15 mg/mL 100 μ Ci	Full Report: *S6–V1.41–P1* Tabulations: *S11–V1.410–P1* CRFs: None	Open, multiple dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood & urine sampling • Saliva sampling • Fecal sampling	Multiple dose 60 mg Q12h: 6 Early DC: 0	6	Population: Healthy subjects Gender: M:F 6:0 Race: Caucasian 6 Age: Range: 21-42 Mean ± SD 30 ± 8	MDL 16,455A 60 mg Q12h X 4 days [14C] MDL 16,455A 60 mg single dose
SEPR0045 JC Kisicki, MD Amendment 1: 5/2/94 Report: K-95-0012-DS Tabulations: K-95-0064-S	Complete (8/15/94 to 9/15/94)	US Terfenadine PG/AA Soln 15 mg/mL [14C] Terfenadine in PG/AA Soln 15 mg/mL 100 μ Ci	Full Report: *S6–V1.49–P1* Tabulations: *S11–V1.410–P104* CRFs: None	Open, multiple dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood & urine sampling • Saliva sampling • Fecal sampling	Multiple dose 60 mg Q12h: 6 Early DC: 0	6*	Population: Healthy subjects Gender: M:F 6:0 Race: Caucasian 6 Age: Range: 20-41 Mean ± SD 30 ± 8	Terfenadine 60 mg Q12h X 4 days [14C] Terfenadine 60 mg single dose

* Number represents terfenadine exposure

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
Dose Proportionality								
PJPR0007 S Harris, MD Amendment 1: 11/5/93 Amendment 2: 11/18/93 Report: K-95-0257-CDS Tabulations: K-95-0258-S	Complete (10/21/93 to 2/19/94)	US MDL 16,455A PG/AA Soln 10 mg/mL MDL 16,455A PG/AA Soln 50 mg/mL MDL 16,455A PG/AA Soln 100 mg/mL	Full Report: *S8–V1.173–P2* Tabulations: *S11–V1.413–P1* CRFs: *S12–V1.446–P272*	DBPC, randomized, 4-period Xover, multiple dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK/PD: • Serial blood & urine sampling • QT_c	Multiple dose PLAC Q12h: 40 40 mg Q12h: 40 200 mg Q12h: 40 400 mg Q12h: 40 Early DC: 1	40	Population: Healthy subjects Gender: M:F 20:20 Race: Caucasian 40 Age: Range: 20-60 Mean ± SD 38 ± 10	Single-blind PLAC Lead-in: Single dose Double-blind PLAC or MDL 16,455A: 6.5 days 14 day washout period between treatments

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0011 JC Kisicki, MD Report: K-94-0770-DS Tabulations: K-94-0771-S	Complete (2/11/94 to 4/24/94)	US Treatment A: MDL 16,455A PG/AA Soln 5 mg/mL Treatment B: MDL 16,455A PG/AA Soln 15 mg/mL Treatment C: MDL 16,455A PG/AA Soln 30 mg/mL Treatment D: MDL 16,455A PG/AA Soln 60 mg/mL	Full Report: *S6-V1.55-P1* Tabulations: *S11-V1.411-P1* CRFs: None	Open, randomized, 4-way Xover, single & multiple dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood & urine sampling	Treatment A: 20 mg single dose, then Q12h: 24 Treatment B: 60 mg single dose, then Q12h: 24 Treatment C: 120 mg single dose, then Q12h: 24 Treatment D: 240 mg single dose, then Q12h: 23 Early DC: 1	24	Population: Healthy subjects Gender: M:F 24:0 Race: Caucasian 22 Black 2 Age: Range: 20-45 Mean ± SD 31 ± 8	Day 1: Single dose Day 3-7: 9 Doses, Q12h 14 day washout between treatments

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Tabulations/ CRFs					
Special Population Pharmacokinetics								
PJPR0013 Investigators (see listing below) Report: K-94-0772-DS Tabulations: K-94-0773-S	Complete (2/17/94 to 7/15/94)	US MDL 16,455A Gelatin Capsules 20 mg (Pilot scale)	Full Report: *S6-V1.73-P1* Tabulations: *S11-V1.422-P1* CRFs: None	Open, stratified by renal function, single dose, multicenter Group I: CrCl= 41-80 mL/min Group II: CrCl= 11-40 mL/min Group III: CrCl ≤ 10 mL/min Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-Lead ECG PK: • Serial blood & urine sampling	80 mg single dose: 29 Group I: 9 Group II: 10 Group III: 10 Early DC: 0	29	Population: Renally impaired subjects Gender: M:F 19:10 Race: Caucasian 20 Black 5 Asian 4 Age: Range: 26-68 Mean ± SD 47 ± 13	Single dose

Study Site	Investigator	No. Entered	Study Site	Investigator	No. Entered
PJST0012	M Horton, PharmD	14			
PJST0013	C Halstenson, PharmD	16			

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Tabulations/ CRFs					
PJPR0020 A Russell, MD Report: K-95-0013-DS Tabulations: K-95-0095-S	Complete (9/12/94 to 9/22/94)	Canada MDL 16,455A Gelatin Capsules 20 mg (Pilot scale)	Full Report: *S6-V1.78-P1* Tabulations: *S11-V1.423-P1* CRFs: None	Open, single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood & urine sampling	80 mg single dose: 20 Early DC: 0	20	Population: Healthy elderly subjects (≥ 65) Gender: M:F 11:9 Race: Caucasian 20 Age: Range: 65-80 Mean ± SD 72 ± 4	Single dose

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0021 Investigators (see listing below) Amendment 1: 5/20/94 Amendment 2: 8/29/94 Amendment 3: 10/12/94 Interim Report: K-95-0169-DS Tabulations: K-95-0170-S	Ongoing (11/16/94 to Interim)	US MDL 16,455A Gelatin Capsules 20 mg (Pilot scale)	Full Report: *S6–V1.80–P1* Tabulations: *S11–V1.423–P158* CRFs: None	Open, stratified by hepatic function, single dose, two center Group I: Child-Pugh Class A Group II: Child-Pugh Classes B & C_1 Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK: • Serial blood & urine sampling	80 mg single dose: 14 Group I: 9 Group II: 5 Early DC: 0	14	Population: Hepatically impaired subjects Gender: M:F 11:3 Race: Caucasian 14 Age: Range: 32-62 Mean ± SD 50 ± 8	Single dose

Study Site	Investigator	No. Entered
PJST0170	S Harris, MD	8
PJST0171	V Luketic, MD	6

fexofenadine hydrochloride capsule

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	Status (Start Date/ Completion Date)	Study Location, Formulation	NDA Data Location: Full Report/ Tabulations/ CRFs	Study Design	Doses, No. Entered Each Treatment	Total Exposed to MDL 16,455A	Demographics	Duration of Drug Treatment
Drug-Drug Interactions								
PJPR0018 D Morrison, DO Amendment 1: 9/28/94 Amendment 2: 11/21/94 Report: K-95-0171-DS Tabulations: K-95-0172-S	Complete (10/8/94 to 12/5/94)	US: Treatment A: MDL 16,455A Gelatin Capsules 60 mg (Full scale) Treatment B: Erythromycin 250 mg Tablets Treatment C: Treatments A and B combined	Full Report: S6-V1.82-P1 Tabulations: S11-V1.424-P1 CRFs: S12-V1.444-P205	Open, randomized, 3-way Xover, multiple dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-Lead ECG PK/PD: • Serial blood & urine sampling • QT_c	Treatment A: 120 mg Q12h: 19 Treatment B: 500 mg Q8h: 21 Treatment C: 120 mg Q12h + 500 mg Q8h: 19 Early DC: 4	20	Population: Healthy subjects Gender: M:F 22:0 Race: Caucasian 21 Black 1 Age: Range: 18-43 Mean±SD 26 ± 7	Treatment A: 6.5 days Treatment B: 6.33 days Treatment C: MDL 16,455A 6.5 days + Erythromycin 6.33 days ≥ 10 day washout period between treatments
PJPR0028 RJ Dockhorn, MD Amendment 1: 9/28/94 Report: K-95-0128-DS Tabulations: K-95-0129-S	Complete (10/5/94 to 11/16/94)	US Treatment A: MDL 16,455A Gelatin Capsules 60 mg (Full scale) Treatment B: Ketoconazole 200 mg Tablets Treatment C: Treatments A and B combined	Full Report: S6-V1.86-P1 Tabulations: S11-V1.426-P1 CRFs: S12-V1.444-P251	Open, randomized, 3-way Xover, multiple dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PK/PD: • Serial blood & urine sampling • QT_c	Treatment A: 120 mg Q12h: 24 Treatment B: 400 mg Q24h: 24 Treatment C: 120 mg Q12h + 400 mg Q24h: 23 Early DC: 2	24	Population: Healthy subjects Gender: M:F 24:0 Race: Caucasian 13 Black 11 Age: Range: 18-45 Mean ± SD 27 ± 8	Treatment A: 6.5 days Treatment B: 7 days Treatment C: MDL 16,455A 6.5 days + Ketoconazole 7 days 10 day washout period between treatments

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
Pharmacodynamics								
PJPR0002 SD Oliver, MD Amendment 1: 6/2/93 Amendment A: 6/4/93 Amendment B: 7/20/93 Report: K-94-0528-CDS Tabulations: K-94-0529-S	Complete (6/93 to 9/93)	UK MDL 16,455A PG/AA Soln 2.5 to 133 mg/mL	Full Report: *S8-V1.133-P2* Tabulations: *S11-V1.428-P1* CRFs: None	DBPC, randomized, parallel, escalating single dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PD: • Skin wheal/ flare • QT_c PK: • Serial blood & urine sampling	Single dose PLAC: 21 10 mg: 6 20 mg: 6 40 mg: 6 80 mg: 6 130 mg: 6 200 mg: 6 280 mg: 6 360 mg: 6 480 mg: 6 640 mg: 6 800 mg: 6 Early DC: 0	66	Population: Healthy subjects Gender: M:F 87:0 Race: Caucasian 87 Age: Range: 18-51 Mean ± SD 27 ± 8	Single-blind PLAC Lead-in: Single dose Double-blind PLAC or MDL 16,455A: Single dose

fexofenadine hydrochloride capsule

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Tabulations/ CRFs					
PJPR0003 SD Oliver, MD Amendment A: 7/20/93 Amendment B: 9/1/93 Report: K-94-0758-CDS Tabulations: K-94 0759-S	Complete (6/93 to 11/93)	UK MDL 16,455A PG/AA Soln 5 to 130 mg/mL	Full Report: *S8-V1.143-P1* Tabulations: *S11-V1.433-P1* CRFs: None	DBPC, randomized, parallel, escalating multiple dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PD: • Serial wheal/ flare • QT_c PK: • Serial blood & urine sampling	Multiple dose PLAC Q12h: 8 20 mg Q12h: 3 40 mg Q12h: 3 80 mg Q12h: 3 160 mg Q12h: 3 260 mg Q12h: 3 390 mg Q12h: 3 520 mg Q12h: 3 690 mg Q12h: 3 Early DC: 1	24	Population: Healthy subjects Gender: M:F 32:0 Race: Caucasian 32 Age: Range: 20-47 Mean ± SD 26 ± 6	Single-blind PLAC Lead-in: Single dose Double-blind PLAC or MDL 16,455A: 28.5 days

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location* — *Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0004 SD Oliver, MD Report: K-94-0776-CDS Tabulations: K-94-0777-S	Complete (8/23/93 to 12/6/93)	UK Treatment E: Seldane® 60 mg Tablets Treatment F: Seldane® 60 mg Tablets Treatment G: MDL 16,455A PG/AA Soln 15 mg/mL Treatment H: MDL 16,455A PG/AA Soln 45 mg/mL	Full Report: *S8–V1.156–P1* Tabulations: *S11–V1.438–P1* CRFs: *S12–V1.445–P1*	Open, randomized, 4 period Xover, multiple dose, single center Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG PD: • Skin wheal/ flare • QT_c PK: • Serial blood & urine sampling	Treatment E: 60 mg Q12h: 23 Treatment F: 180 mg Q12h: 23 Treatment G: 60 mg Q12h: 24 Treatment H: 180 mg Q12h: 23 Early DC: 2	24	Population: Healthy subjects Gender: M:F 24:0 Race: Caucasian 23 Black 1 Age: Range: 20-51 Mean ± SD 30 ± 2	Treatment E: 6.5 days Treatment F: 6.5 days Treatment G: 6.5 days Treatment H: 6.5 days 15 day washout period between treatments

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/. Completion Date)*	*Study Location, Formulation*	*NDA Data Location* — *Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
PJPR0017 J Day, MD Amendment 1: 10/26/94 Amendment 2: 11/2/94 Amendment 3: 11/23/94 Report: K-95-0041-CS Tabulations: K-95-0042-S	Complete (11/25/94 to 12/11/94)	Canada MDL 16,455A Gelatin Capsules 60 mg	Full Report: *S8–V1.166–P1* Tabulations: *S11–V1.442–P1* CRFs: None	DBPC, randomized, parallel, single dose, single center Efficacy: • Onset of action Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals	Single dose PLAC: 33 60 mg: 33 120 mg: 33 Early DC: 0	66	Population: RPAR patients Gender: M:F 38:61 Race: Caucasian 94 Asian 4 Other 1 Age: Range: 14-62 Mean ± SD 31 ± 13	Single-blind PLAC Lead-in: Single dose Double-blind PLAC or MDL 16,455A: Single dose

Table 8–7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location: Full Report/ Tabulations/ CRFs*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
Effect of Gastric pH								
016455PR0022 (PJPR0022) WS Nimmo, MD Amendment 1: 3/3/95	Ongoing	UK Treatment A: MDL 16,455A Gelatin Capsules 60 mg Treatment B: Omeprazole 20 mg followed 10h later by Omeprazole 40 mg followed 1h later by MDL 16,455A Gelatin Capsules 60 mg Treatment C: 20 mL Maalox followed 15 min later by MDL 16,455A Gelatin Capsules 60 mg	Full Report: N/A Tabulations: N/A CRFs: N/A	Open, randomized, 3-way Xover, single dose, single center Safety • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG (screen only) PK/PD • Serial blood sampling • pH	Treatment A: 120 mg Treatment B: Omeprazole + 120 mg Treatment C: Maalox + 120 mg	Planned: 24	Population: Healthy subjects	All Treatments: Single dose >5 day washout between treatments

fexofenadine hydrochloride capsule

Table 8-7. Table of All Clinical Pharmacology Studies

Protocol No., Investigators, Protocol Amendments, Report No., Publications	*Status (Start Date/ Completion Date)*	*Study Location, Formulation*	*NDA Data Location*	*Study Design*	*Doses, No. Entered Each Treatment*	*Total Exposed to MDL 16,455A*	*Demographics*	*Duration of Drug Treatment*
			Full Report/ Tabulations/ CRFs					
Psychomotor Performance								
01645PR0030 (PJPR0030) J F O'Hanlon	Ongoing	Netherlands MDL 16,455A Gelatin Capsules 60 mg Clemastine Tablets 2 mg	Full Report: N/A Tabulations: N/A CRFs: N/A	DBPC, randomized, 6-way Xover, multiple dose, single center Efficacy: • Psychometric, psychomotor performance Safety: • Treatment-emergent AEs • PE, Clin Lab, Vitals • 12-lead ECG	PLAC, 60, or 120 mg Q12h Clemastine 2 mg daily	Planned: 24	Population: Healthy Subjects	5 days

A. Biopharmaceutics Study Summary Table

Table 6-1. **Biopharmaceutics Study Summary**
(Page 1 of 10)

IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
Bioavailability/Bioequivalence							
PJPR0001 K-95-0061-DS *S6-V1.22-P2*	Oral	Single dose bioavailability, formulation screen, 3-period complete crossover	22.5 mg/mL sol 30 mg uncoated tab (wet granulation) 6 mg/mL micellular sol	90 mg 90 mg 90 mg	FR MDL 16,455A-21 4/93 UK WN930613 6/93 UK WN930606 6/93	24 healthy males	Relative Bioavailability of micellular solution and prototype tablet were 106% and 71%, respectively, relative to a PG/AA solution based on adjusted mean.
PJPR0005 K-95-0050-DS *S6-V1.25-P1*	Oral	Single dose bioavailability, formulation screen, 3-period complete crossover	22.5 mg/mL sol 30 mg uncoated tab (direct compression) 30 mg gelatin cap	90 mg 90 mg 90 mg	FR MDL 16,455A-21 4/93 UK WN930824 8/93 UK WN930816 8/93	24 healthy males	Relative Bioavailability of prototype capsule and tablet were 87% and 70.1%, respectively, compared to a PG/AA solution based on adjusted mean.
PJPR0012 K-94-0768 DS *S6-V1.28-P1*	Oral	Single dose bioavailability, food interaction, repeated treatment, 5-period crossover.	20 mg/mL sol 20 mg gelatin cap	80 mg 80 mg	US 73038 10/93 US RN9323 1/94	24 healthy males	No pharmacokinetic analysis performed due to incorrect handling of plasma samples at the site, compromising bioanalytical results.

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6–1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
PJPR0015 K-94-0742-CDS *S6-V1.30-P1*	Oral	Single dose bioavailability, tablet screen, 4-period crossover, six treatment incomplete block	22.5 mg/mL sol	90 mg	US 73038 10/93	30 healthy males	Relative bioavailability of all formulations was greater than 81.32%, compared to a reference PG/AA solution based on adjusted mean.
			30 mg gelatin cap	90 mg	US RB9430 3/94		
			30 mg gelatin cap with Mg stearate;	90 mg	US RB9429 3/94		
			30 mg coated tab with Mg stearate;	90 mg	US RC9403 3/94		
			30 mg coated tab without gelatin;	90 mg	US RB9420 3/94		
			30 mg coated tab	90 mg	US RB9424 3/94		
PJPR0025 K 95-0034 DS *S6-V1.32-P1*	Oral	Single dose pivotal bioavailability, bioequivalence, 5-period three treatment crossover, repeated treatment.	30 mg/mL sol	120 mg	US 73038 10/93	24 healthy males	60 mg full-scale capsule and 20 mg pilot-scale capsule were bioequivalent to each other and were bioequivalent to the oral reference PG/AA solution based on adjusted mean AUC and Cmax.
			20 mg gelatin cap (pilot scale)	120 mg	US RN9323 1/94		
			60 mg gelatin cap (full scale)	120 mg	US RF9414 7/94		
PJPR0026 K-95-0109-DS *S6-V1.35-P1*	Oral	Single dose food interaction; manufacturing spec (particle size/ surface area variation), 5-period complete crossover.	40 mg gelatin caps SA: 3.80 m^2/gm upon fasting;	80 mg	US RF9422 7/94	25 healthy males	Food decreased adjusted mean AUC and Cmax of tablet by 17% and 11%, respectively; results of manufacturing specification will be reported later.
			SA: 3.80 m^2/gm; with food;	80 mg	US RF9422 7/94		
			SA: 2.84 m^2/gm upon fasting;	80 mg	US RJ9415 10/94		
			SA: 1.92 m^2/gm upon fasting;	80 mg	US RJ9413 10/94		
			SA: 1.05 m^2/gm upon fasting	80 mg	US RJ9409 10/94		

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6-1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
PJPR0029 K-95-0165-DS *S6-V1.37-P1*	Oral	Single dose, bioequivalence; food interaction, 5-period complete three treatment crossover, repeated treatment	40 mg gelatin cap 40 mg coated tab with Mg stearate upon fasting 40 mg coated tab with Mg stearate with food	120 mg 120 mg 120 mg	US RF9422 7/94 US RM9414 11/94 US RM9414 11/94	24 healthy males	Full-scale capsule and tablet formulation were bio-equivalent; food decreased adjusted mean AUC and C_{max} of tablet by 24% and 25%, respectively.
Mass Balance / Metabolism							
PJPR0008 K-94-0833-DS *S6-V1.41-P1* K-94-0869-D *S6-V1.47-P1*	Oral	Multiple dose mass balance for 4.5 days twice daily - MDL 16,455A single group design	15 mg/mL sol (8 doses) followed by 15 mg/mL [14C] sol (1 dose)	60 mg Q12 h 60 mg [14C]	US 73038 10/93 US 73136 10/93	6 healthy males	91.52% of the dose was recovered from feces (80.04%) and urine (11.48%); MDL 16,455 only major species identified.
SEPR0045 K-95-0012-DS *S6-V1.49-P1* K-95-0233-D *S6-V1.53-P1*	Oral	Multiple dose mass balance for 4.5 days twice daily - terfenadine single group design	15 mg/mL sol (8 doses) followed by 15 mg/mL [14C] sol (1 dose)	60 mg Q12 h Terfenadine 60 mg [14C] Terfenadine	US 72954 9/92 US 74788 5/94	6 healthy males	93.16% of the dose was recovered from feces (51.64%) and urine (41.52%); 47.25% dose excreted as MDL 16,455.

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6-1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
Pharmacokinetics / Dose Proportionality							
PJPR0011 K-94-0770-DS *S6-V1.55-P1*	Oral	Single dose, & multiple dose (twice daily dosing for 4.5 days) proportionality; assessment of total MDL 16,455 and its R(+) & S(-) enantiomers, 4-period complete crossover	5 mg/mL sol 15 mg/mL sol 30 mg/mL sol 60 mg/mL sol	20 mg Q12 h 60 mg Q12 h 120 mg Q12 h 240 mg Q12 h	US 73038 10/93	24 healthy males	MDL 16,455 pharmacokinetics following single and multiple doses of 20 to 120 mg were linear; slight disproportionate increases in AUC and C_{max} were observed at 240 mg. Plasma concentration ratio of R(+) to S(-) MDL 16,455 is 63:37 for all doses. Single dose pharmacokinetics predictive of steady-state adjusted mean AUC.
PJPR0007 K-95-0257-CDS *S6-V1.61-P1*	Oral	Multiple dose proportionality, dosing for 6.5 days twice daily (13 doses)	10 mg/mL sol 50 mg/mL sol 100 mg/mL sol	40 mg Q12 h 200 mg Q12 h 400 mg Q12 h	US 73038 10/93	20 healthy males and 20 healthy females	Slight disproportionate increases in AUC_{ss}, $C_{max,ss}$, $C_{min,ss}$, and amount excreted were observed over the 10-fold range; AUC_{ss}, $C_{max,ss}$, and amount excreted were greater (33%-46%) in women than in men, across all doses based on adjusted mean.

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6-1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
Special Population							
PJPR0013 K-94-0772-DS *S6-V1.73-P1*	Oral	Single dose, renally impaired subjects with varying degrees of renal disease	20 mg gelatin cap (pilot scale batch)	80 mg	US RN9323 1/94	19 males and 10 females	Plasma MDL 16,455 pharmacokinetics appeared to be independent of the severity of renal disease, but adjusted mean AUC (0-∞) was 88.53% higher than that generally observed in healthy males from separate studies; urinary excretion declined with increasing severity of disease.
PJPR0020 K-95-0013-DS *S6-V1.78-P1*	Oral	Single dose, elderly subjects range 65 to 80 (mean 72) years	20 mg gelatin cap (pilot scale batch)	80 mg	US RB9434 3/94	11 males and 9 females	Adjusted mean AUC (0-∞) was 62.52% higher than that in young subjects from separate studies.
PJPR0021 K-95-0169-DS *S6-V1.80-P1*	Oral	Single dose, hepatically impaired subjects (Classes A, B, and C1)	20 mg gelatin cap (pilot scale batch)	80 mg	US RB9432 2/94	11 males and 3 females	Plasma pharmacokinetic parameters less than 25% different from normal subjects.

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6-1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
Drug Interaction							
PJPR0018 K-95-0171-DS *S6-V1.82-P1*	Oral	Three-period complete crossover, multiple doses of MDL 16,455A and/or erythromycin for 6.5 days	60 mg MDL 16,455A gelatin cap 250 mg erythromycin tab (alone and in combination)	120 mg (Q 12h) 500 mg (Q 8 h)	US RH9411 8/94 US 743KP N/A (Supplied by Site)	24 healthy males	Erythromycin increased MDL 16,455 adjusted mean AUC_{ss} and $C_{max,ss}$ by 103.38% and 80.37%, respectively. MDL 16,455 had no effect on pharmacokinetics of erythromycin; no effect on safety parameters including QT_C.
PJPR0028 K-95-0128-DS *S6-V1.86-P1*	Oral	Three-period complete crossover, multiple doses of MDL 16,455A and/or ketoconazole for 6.5 days	60 mg MDL 16,455A gelatin cap 200 mg ketoconazole tab (alone and in combination)	120 mg (Q 12h) 400 mg (Q 24h)	US RH9411 8/94 US 94J453E N/A (Supplied by Site)	24 healthy males	Ketoconazole increased adjusted mean AUC_{ss} and $C_{max,ss}$ by 159.31% and 129.86%, respectively. MDL 16,455 had no effect on ketoconazole; no effect on safety parameters including QT_C.

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
†: FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6–1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
Population Pharmacokinetics							
PJPR0023 Clinical Report: K-95-0005-CDS *S8-V1.219-P1*	Oral	Double-blind randomized placebo-controlled, parallel safety and efficacy study	60 mg gelatin cap	60 mg Q12 h 120 mg Q12 h 240 mg Q12 h	US RF9414 7/94	176 males & 241 females	Gender effect was the only significant covariate affecting pharmacokinetics of MDL 16,455. CL_{po} of males was 14% to 17% higher than females. Patient, age, race, and concomitant medications had no effects. MDL 16,455A was dose proportional over the 40 mg to 240 mg BID range in patients.
PJPR0024 Clinical Report: K-95-0007-CDS *S8-V1.239-P1*	Oral	Double-blind randomized placebo-controlled, parallel safety and efficacy study	Combination of : 20 mg and 40 mg gelatin cap	40 mg Q12 h 60 mg Q12 h 120 mg Q12 h	US RB9434 3/94 US RF9422 7/94	158 males & 251 females	
PJPR0023/ PJPR0024 Pharmacokinetic Report: K 95-0154-DS *S6-V1.89-P15*	Oral	Patients on MDL 16,455A analyzed from both studies	See above two studies	40 mg Q12 h 60 mg Q12 h 120 mg Q12 h 240 mg Q12 h	See above two studies	306 males & 453 females Note: Not all subjects produced plasma samples.	

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6–1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
Pharmacodynamic/Safety/Dose Tolerance							
PJPR0002 K-94-0528-CDS *S6-V1 93-P1*	Oral	Single dose safety trial, parallel group escalating doses	2.5 mg/mL sol 5 mg/mL sol 10 mg/mL sol 20 mg/mL sol 32.5 mg/mL sol 50 mg/mL sol 70 mg/mL sol 90 mg/mL sol 120 mg/mL sol 107 mg/mL sol 133 mg/mL sol	10 mg 20 mg 40 gm 80 mg 130 mg 200 mg 280 mg 360 mg 480 mg 640 mg 800 mg	FR MDL 16,455A-20 4/93 FR MDL 16,455A-20 4/93 FR MDL 16,455A-20 4/93 FR MDL 16,455A-20 4/93 FR MDL 16,455A-20 4/93 FR MDL 16,455A-20 4/93 FR MDL 16,455A-20 4/93 FR MDL 16,455A-20 4/93 FR MDL 16,455A-21 4/93 FR MDL 16,455A-21 4/93 FR MDL 16,455A-21 4/93	66 healthy males on active drug (6 per dose level)	No dose-related increases in adverse events, QT_c, and laboratories were observed, and the maximum tolerated dose was not attained; MDL 16,455A was rapidly absorbed and exhibited multi-expontential distribution and elimination; individual subject exposure was as high as 12,250 ng/mL; MDL 16,455A antihistaminic activity as measured by skin wheal/flare was observed at doses ≥20 mg, with maximum response achieved at 130 mg.

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6–1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
PJPR0003 K-94-0758-CDS *S6-V1.103-P1*	Oral	Multiple dose twice daily for 28.5 days, safety trial, parallel group escalating doses	5 mg/mL sol 10 mg/mL sol 20 mg/mL sol 40 mg/mL sol 65 mg/mL sol 97.5 mg/mL sol 130 mg/mL sol 115 mg/mL sol	20 mg Q12 h 40 mg Q12 h 80 mg Q12 h 160 mg Q12 h 260 mg Q12 h 390 mg Q12 h 520 mg Q12 h 690 mg Q12 h	FR MDL 16,455A-20 4/93 FR MDL 16,455A-20 4/93 FR MDL 16,455A-20&21 4/93 FR MDL 16,455A-21 4/93 FR MDL 16,455A-21 4/93 FR MDL 16,455A-21 4/93 FR MDL 16,455A-21 4/93 FR MDL 16,455A-21 4/93	24 healthy males on active drug (3 per dose level)	No dose-related increases in adverse events, QT_C, and laboratory values were observed, and the maximum tolerated dose was not attained; steady-state was reached by day 5; $C_{max,ss}$ and AUC_{ss} generally increased proportional to dose; MDL 16,455A antihistaminic activity as measured by skin wheal/flare was observed at all doses, with a maximum response achieved at 160 mg.

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Table 6–1. Biopharmaceutics Study Summary
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IND No. 43,573 Protocol No. Report No.	*Route*	*Study Design*	*Dosage Form(s)*	*MDL 16,455A Dose*	*Plant (Country)* † Lot No. Date of Manufacture*	*Number of Subjects Exposed*	*Applicant Conclusion*
PJPR0004 K-94-0776-CDS *S6-V1.116-P1*		Multiple dose for 7.5 days twice daily: assessment of total	15 mg/mL and 45 mg/mL MDL 16,455A sol	60 mg Q12 h and 180 mg Q12 h	FR MDL 16,455A-21 4/93	24 healthy males	MDL 16,455A had no effect on QT_c, while terfenadine effected an increase in QT_c; antihistaminic effect of both drugs as assessed by skin wheal and flare was similar; MDL 16455 AUC_{ss} after MDL 16,455A was 75% of that following terfenadine administration.
K-95-0070-D *S6-V1.89-P1*	Oral	MDL 16,455 and its R(+) & S(-) enantiomers	60 mg terfenadine tabs	60 mg Q12 h and 180 mg Q12 h	US 0242AE 6/91		No difference between the ratio of MDL 16,455 enantiomers following MDL 16,455A or terfenadine administration.

sol: MDL 16,455A solution in 1.5% glacial acetic acid/98.5% propylene glycol prepared at the clinic site from bulk drug provided by the Sponsor (PG/AA)
cap: hard gelatin capsule formulation
tab: tablet formulation
*: FR - Limay (France); UK - Winnerish (United Kingdom); US - Kansas City (United States)
N/A: not applicable
† FR MDL 16,455A-20 is the same as Limay Lot No. 113-10; FR MDL 16,455A-21 is the same as Limay Lot No. 93-1.

Date 08/06/96

Time 11.18.44

Contact Tracking/FDA Review
All Corresp/Submission/Contacts To/From FDA
Product History Log From 07/31/95 To 07/31/96
FEXOFENADINE HYDROCH
NDA Number 20-625

REGCTR05

Submission Date	Log Number IND/NDA:Date	Origin/ Type	Classi- fication	Supp/ Serial#	Description/ Comments
95/07/31	20-625:950731	NMD Sub	ALL		SUBMIT NEW NDA/ TAH NDA, DELIVERED BY J.DUNN 454 VOLUMES LSK
	20-625:950731A	NMD Sub	ALL		PATENT INFO AND DECLARATION/ AS WELL AS SUBMITTING IN THE NEW NDA, SENT PATENT LETTERS SEPARATELY TO FILE ROOM.
	20-625:950731B	NMD Tel	ALL		FEXOFENADINE HCI: #5,375,693, AND #4,254,129. LSK
95/08/01	20-625:950801	NMD Ltr	CHC		CONTACT:CKY/KLEE:NDA COMING/ CINDY CALLED KLEE TO INFORM HIM THAT THE NDA WAS COMING. AEF
	20-625:950801A	NMD Tel	ALL		LTR:JJD/WMROGERS:SECTION 3 TAH/ JACK SENT W MICHAEL ROGERS OF THE FDA A COPY OF SECTION 3 OF THE TAH NDA. AEF
	20-625:950801B	FDA Tel	Other		CONTACT:CKY/MSEVKA:NDA/SEL/ CINDY CONTACTED MIKE SEVKA TO INFORM HIM THAT THE NDA SHOULD HAVE BEEN RECEIVED BY THE DOC CONTROL ROOM 7/31. SELDANE/SELDANE-D ISSUES WERE ALSO DISCUSSED. AEF
95/08/02	20-625:950802	NMD Ltr	Other		CONTACT:KLEE/CKY:DESK COPY/ KLEE TELEPHONED TO DETERMINE IF AN ADDITIONAL COPY OF THE EA COULD BE FORWARDED TO THE DIVISION. AEF
95/08/03	20-625:950803	NMD Tel			LTR:CKY/MSEKVA:APP SUMM/ CINDY SENT LETTER TO ALERT MSEVKA THAT A COPY OF THE APPLICATION SUMMARY (DESK COPY) IS COMING TO HIM AS REQUESTED. AEF
	20-625:950803A				DISCUSS A.LISOOK PJPR0024/ CONTACTED A.LISOOK, FDA, TO DISCUSS SYMPTOM DIARY PROBLEMS AND RELATED DATA INTEGRITY ISSUES WITH C.LAFORCES SITE FOR PJPR0024.
95/08/04	20-625:950804	NMD Ltr	Other		CONTACT:CKY/KLEE:ENV ASSESSMEN/ CINDY SENT A DESK COPY OF THE ENVIRONMENTAL ASSESSMENT TO K LEE. AEF

Contact Tracking/FDA Review
All Corresp/Submission/Contacts To/From FDA
Product History Log From 07/31/95 To 07/31/96
FEXOFENADINE HYDROCH
NDA Number 20-625

Submission Date	Log Number IND/NDA:Date	Origin/ Type	Classi- fication	Supp/ Serial#	Description/ Comments
95/08/04	20-625:950804A	FDA Tel	Other		CONTACT:SWILSON/CKY:CANDA/ STEVE WILSON CALLED TO INFORM CINDY THAT IF IT TAKES 1.5 HOURS PER WORK STATION HE WOULD RECOMMEND COMING IN ON 8/17. AEF
	20-625:950804B	MMD Tel	Other		CONTACT:CKY/KLEE:CANDA/ CINDY CONTACTED KLEE TO INFORM HIM THAT THE INSTALLATION OF THE CANDA WOULD BE 8/17/95. AEF
95/08/07	20-625:950807	FDA Tel	ALL		CONTACT:KLEE/CKY:NDA COPIES/ KLEE PHONED TO REQUEST ADDITIONAL COPIES OF THE NDA FOR DR HIMMEL. AEF
95/08/08	20-625:950808	MMD Sub	Expert		REQUEST EXPORT APPLICATION/ REQUEST APPROVAL OF EXPORT APPLICATION FOR TELFAST TABS TO FRANCE FOR PKG, THEN TO THE U.K. FOR MARKETING. LSK
95/08/09	20-625:950809	MMD Tel	Other		CONTACT:CKY/KLEE:TAM D - CANDA/ CINDY CONTACTED KLEE TO SEE IF THE TAM-D IND WAS RECEIVED. ALSO DISCUSSED WAS THE CANDA INSTALLATION FOR TAM. AEF
95/08/14	20-625:950814	FDA Tel	Other		CONTACT:KLEE/CKY:CANDA/ KLEE PHONED TO DETERMINE THE STATUS OF THE CANDA INSTALLATION. AEF
	20-625:950814A	MMD Ltr	ALL		LTR:CKY/KLEE:REQUESTED COPIES/ CINDY SENT KLEE DESK COPIES OF SECTION 1,6,8 AS REQUESTED BY FDA. AEF
95/08/15	20-625:950815	MMD Sub	Clinical		RESUBMIT VOLUME 1.219/ 80 PAGES LEFT OUT OF ORIGINAL VOLUME SENT TO FDA ON 7/31/95. RESENT THIS VOLUME TO FDA. LSK

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95/08/17	20-625:950817	MMD Tel	Other		CONTACT:CKY/KLEE:FOLLOW-UP/ CINDY CONTACTED KLEE TO FOLLOW-UP INFO REGARDING FUTURE PLANS FOR SELDANE/ SELDANE-D. AEF
	20-625:950817A	MMD Tel	Other		COPY OF DATA FROM 19-664:950817 CONTACT:CKY/KLEE:CANDA INSTALL/ CINDY CONTACT KOUNG TO INFORM HIM THAT THE IS PEOPLE WOULD BE ARRIVING TODAY TO INSTALL THE EQUIPMENT FOR CANDA. AEF
95/08/27	20-625:950827	FDA Tel	Clinical		CONTACT:GTURNER/CKY:THANK YOU/ GUS TURNER CALLED TO THANK CINDY FOR THE RECENT SUBMISSION ON SITE 155. AEF
95/08/28	20-625:950828	MMD Ltr	Other		CONFIRM TRAINING ARRANGEMENTS/ LETTER TO CONFIRM THE ARRANGEMENTS FOR THE CANDA TRAINING WORKSHOPS ON 8/29 AND 9/6/95. LSK
95/09/05	20-625:950905	MMD Ltr	Other		LTR:CKY/KLEE/SUBMISSION COPY/ COVER LTR FROM CKY TO KLEE SENDING SUBMISSION COPIES OF FEXOFENADINE HYDROCHLORIDE CAPSULES-SUPPORT STATISTICAL ANALYSIS PROGRAMS, DATASETS AND DOCUMENTATION. DESK COPY PROVIDED AT SEPTEMBER 6, 1995 CANDA MEETING.
95/09/06	20-625:950906	MMD Mtg	Labeling Other		TRAINING FOR CANDA/ TRAINING SET 9/6/95 (SESSION 2), SESSION 1 HELD ON 8/27/95. OBJECTIVES WERE TO DETERMINE PREFERRED FORMAT FOR 4-MONTH SAFETY UPDATE, LEVEL OF IS SUPPORT FOR CANDA AND STATUS OF NDA REVIEW.

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FEXOFENADINE HYDROCH
NDA Number 20-625

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95/09/06	20-625:950906A	MMD Tel	GMP		FEXOFENADINE PRE-APPROVAL INSP/ TELEPHONE CALL TO FDA INQUIRING ABOUT THE PRE-APPROVAL INSPECTION FOR FEXOFENADINE. DICKINSON WOULD NOT COMMIT UNTIL SHE TALKED WITH M. GARZA
95/09/08	20-625:950908	MMD Ltr	Other		FOLLOW-UP TO FDA REQUEST/ DESK COPY AND ACCOMPANYING ELECTRONIC COPY (DISKETTE) TO KLEE OF INFORMATION PREVIOUSLY SUBMITTED TO NDA 20-625 ON 9/5/95.
	20-625:950908A	MMD Tel	Clinical		FOLLOW-UP TO MEETING OF 9/6/95/ CALLED SEVKA TO FOLLOW-UP ON REQUESTS FROM 9/6/95 MEETING. ADVISED THAT THE INVESTIGATORS USED IN FEXOFENDADINE TRIALS WERE NOT BLACKLISTED. ALSO ADVISED THAT CMC AMENDMENT WAS SUBMITTED ON 9/7 AND WE WOULD APPRECIATE A RAPID REVIEW.
95/09/11	20-625:950911	MMD Ltr	ALL		DESK COPY-RESPONSE TO REQUEST/ CKIRK-YOURTEE SENT TO KLEE DESK COPY OF PREVIOUSLY SUBMITTED INFO - WORD-PERFECT FILES AS REQUESTED PREVIOUSLY BY DRS SEVKA AND WILSON.
95/09/13	20-625:950913	MMD Tel	Other		MULTISOURCE SCENARIO CHANGE/ DRS SEVKA AND LEE CALLED TO DISCUSS OUR REQUEST FOR A MEETING TO DISCUSS THE CHANGED SCENARIO FOR MULTISOURCES OF TERFENADINE. (DDA)
95/09/14	20-625:950914	FDA Tel	Other		DATA TRANSFER/ENDA TO ACCESS/ DR SEVKA CALLED TO SEE IF IT WOULD BE POSSIBLE TO TRANSPORT DATA FROM THE ENDA TO ACCESS FILES FOR THE 4 PIVOTAL TRIALS.(DDA)

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95/09/18	20-625:950918	HMD Tel	Other		SCHEDULE ENDA MEETING/ CALLED KOUNG LEE TO SET TIME FOR ENDA MEETING WITH SALLY KORTY AND BARBAR BONO BUT HE ADVISED THAT BARBARA HAD FIGURED OUT THE PROBLEM AND THERE WAS NO NEED FOR A MEETING. (DDA)
95/09/20	20-625:950920	HMD Tel	Other		PROGRESS OF FILING FEX-NDA/ CALLED TO DISCUSS PROGRESS OF FILING THE FEX NDA AND NOTED THAT WE WERE AT THE 45 DAY FILING MARK.(DDA)
95.09.21	20-625:950921	FDA Tel	Clinical		DATA INTEGRITY/STUDIES/INVEST/ GUS TURNER CALLED TO SAY THAT DR SEVKA HAD ASKED HIM TO DETERMINE SPECIFICS REGARDING DR LAFORCE AND CONCERNS FOR DATA INTEGRITY AND INFORMATION ON THE STUDIES AND INVESTIGATORS IN THE NDA. (DDA)
	20-625:950921A	FDA Tel	Other		CONTACT:BBONO/SAK:ENDA PROBLEM/ BARBARA BONO CALLED SALLY KORY ABOUT A PROBLEM WITH THE ENDA. AEF
95.09.22	20-625:950922	HMD Ltr	Other		RESPONE TO FDA REQUEST: CKY/ PER REQUEST OF 9/21/95, CKIRK-YOURTEE SENT TO GURSTON TURNER DESK COPY OF INFO PREVIOUSLY SUBMITTED IN ORIGINAL NDA 20-615: APPLICATION SUMMARY; SEC 2, VOL 1.1 PP 1-363. LIST OF CLIN PROTOCOLS SEC 2, VOL 1.1 P 298. DESCRIP PJPR0024 SITE 155 OBSERV. SEC 8, VOL 1.239 P 60. LIST OF INV.-SEC 8, VOL 1.132 P 14-63.LG
	20-625:950922A	FDA Tel	Clinical Labeling Other		CONTACT:KLEE/CKY:MISC/ KOUNG CALLED TO REQUEST ASSISTANCE FOR MIKE SEVKA AND BARBARA BONO. SELDANE, SELDANE-D, TAH-D WERE ALSO DISCUSSED. AEF

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95/09/25	20-625:950925	FDA Tel	Biopharm Clinical		CONTACT:CKY/KLEE:ENDA/SAS/ CINDY, SALLY KORTY(HMR), STEVE WILSON (FDA), KOUNG LEE (FDA) AND BARBARA BONO (FDA) HAD A TELECON RE: ENDA TO SAS FILES. AEF
	20-625:950925A	FDA Tel	Other		CONTACT:KLEE/CKY:ADDITI REQUES/ KLEE PHONED WITH ADDITIONAL REQUESTS. NEEDED CONFIRMATION OF THE SITES FOR DRUG SUBSTANCE MANUFACTURE, PRODUCT MANUFACTURE AND PACKAGING/STABILITY RELEASE. AEF
95/09/26	20-625:950926	MMD Ltr	Clinical		RESP. TO FDA REQ. 2 COPIES WP/ TWO COPIES OF WORDPERFECT 6.0A VERSIONSX OF NDA 20-625 PROTOCOLS AND PAPER COPY. PROTOCOLS PREVIOUSLY SUBMITTED IN NDA. PJPR0003, 004, 007, 009, 010, 017, 018, 023, 024, 028. LJG
	20-625:950926A	FDA Tel	Clinical		CONTACT:BBONO/SAK:PATDIARY/ BARBARA BONO PHONED SALLY KORTY TO ASK ABOUT PATDIARY DATA. AEF
	20-625:950926B	FDA Tel	Clinical		CONTACT:CKY/KLEE:INFO REQUEST/ KOUNG LEE, BARBARA BONO, MIKE SEVKA CALLED CINDY REQUESTING INFORMATION ON PJPR0024, SITE 155. AEF
95/09/27	20-625:950927	MMD Sub	ALL		TRADENAME - ALLEGRA/ TRADENAME FOR FEXOFENADINE HCL IDENTIFIED AS ALLEGRA(TM). LJG
	20-625:950927A	FDA Tel	Biopharm		CONTACT:BGILLESPIE/CKY:NOMEM/ BRAD GILLESPIE CALLED TO ASK FOR INFO ON THE NOMEM POPULATION STUDY OF PJPR0023/24. AEF
	20-625:950927B	FDA Fax	Other		FAX:KLEE/CKY:SAMPLE LETTER/ KOUNG LEE SENT CINDY FAX OF SAMPLE LETTER FOR LOANING EQUIPMENT/SOFTWARE TO CDER. AEF

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95/09/27	20-625:950927C	FDA Tel	Clinical Other		CONTACT:KLEE/CKY:CANDA BACK-UP/ KLEE PHONED TO INFORM CINDY THAT THE DIVISION IS INTERESTED IN THE CANDA BACK-UP PLAN. TAM-D 180 MG PROTOCOL WAS ALSO DISCUSSED. AEF
	20-625:950927D	HMD Tel	GMP		CALL TO FDA ON PREAPPOVAL INSP/ CALL TO GARZA TO CONFIRM OUR READINESS FOR THE PRE-APPROVAL INSPECTION FOR THE FEXOFENADINE CAPSULE NDA AND DILTIAZEM TABLET SUPPLEMENT TO THE NDA.
95/09/28	20-625:950928	HMD Ltr	Clinical		DISKETTES HOLMEM DATA FILES/ 2 COPIES OF DISKETTES CONTAINING HOLMEM DATA FILES FROM NDA S6-VI.89-P84.
	20-625:950928A	HMD Ltr	Clinical		DESK COPY FOR DR GILLESPIE'S USE. LJG 2 COPIES 10 DISKETTES - AES/ REF: SEVKA & BOHO'S REQUEST OF 9/26/95 2 COPIES OF 10 DISKETTES - ADVERSE EVENTS, ALL TREATMENT RELATED ADVERSE EVENT ALL ECG READINGS AND LAB DATA.
	20-625:950928B	HMD Ltr	Clinical		DATA PROVIDED PREVIOUSLY SUBMITTED IN ORIGINAL NDA. LJG RESPONSE TO 9/27 REQ. ADD'L IN/ CKY RESPONSE TO GTURNER REQUEST OF 9/27/95 FOR ADD'L INFORMATION ON PROTOCOL PJPR0024 SITE PJST0155 OF NDA. LJG
95/10/03	20-625:951003	HMD Ltr	ALL		INTENT PROVIDE CANDA SYSTEM/ TO DAVE MOSS, SUPERVISORY COMPUTER SPECIALIST - NOTICE OF INTENT TO PROVIDE CANDA SYSTEM TO CDER. LJG
95/10/04	20-625:951004	HMD Ltr	ALL		REPLACEMENT LTR: CANDA/ REVISED LETTER AS REPLACEMENT TO LETTER DATED 10/3/95 RE: NOTICE OF INTENT TO PROVIDE CANDA SYSTEM TO CDER. LJG

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95/10/06	20-625:951006	NMD Sub	Labeling		PI WORDPERFECT 6.0A/ANN/NONANN/ PER FDA REQUEST SUBMITTED PRESCRIBING INFORMATION TRANSLATED TO WORDPERFECT 6.0A - BOTH ANNOTATED (LABELANN.WP6) AND NON-ANNOTATED (LABELNON.WP6) VERSION ON DISKETTE AND HARDCOPY. LJG
	20-625:951006A	FDA Tel	Clinical Other		CONTACT:KLEE/CKY:PASSES/ KOUNG LEE CALLED TO INFORM CINDY THAT HE HAD THE PROPERTY PASSES FOR THE CANDA. TAM-D WAS ALSO DISCUSSED. AEF
95/10/10	20-625:951010	NMD Tel	Other		CONTACT:DSTALEY/KLEE:INSTALL/ OCTOBER 10, DEBORAH STALEY INSTALLED CANDA EQUIPMENT FOR BARBARA BONO, SHE ALSO TOOK EQUIPMENT FROM NANCY SMITH'S OFFICE. AEF
95/10/13	20-625:951013	FDA Tel	Clinical		CONTACT:BGILLESPIE/CKY:ANOVA/ BRAD GILLESPIE PHONED TO REQUEST DATA FOR PJPR0025. AEF
	20-625:951013A	FDA Tel	Clinical		CONTACT:GTURNER/CKY:AUDITS/ GUS TURNER PHONED TO INFORM CINDY THAT HE IS PREPARING FOR STUDY SITE AUDITS. AEF
	20-625:951013B	FDA Tel	Other		CONTACT:BBONO/SAK:PROBLEM/ BARBARA BONO CALLED SALLY KORTY TO REPORT PROBLEMS EXPORTING DATA ON THE ENDA. AEF
95/10/16	20-625:951016	NMD Tel	Clinical		CONTACT:JJD/GTURNER:CLARIFY/ JACK CALLED GUS TURNER TO CLARIFY HIS REQUEST OF 10/13/95 RE: PATIENTS IN THE FEX PIVOTAL STUDIES. AEF
	20-625:951016A	NMD Ltr	Other		RESP. TO BGILLESPIE REQ./ RESPONSE TO BGILLESPIE'S REQUEST OF 10/13/95 RE: SAS PROGRAM. LJG
	20-625:951016B	FDA Ltr	ALL		FDA FILED NDA 9/28/95/ NEW DRUG APPLICATION RECEIVED 7/31/95 AND FILED 9/28/95. LJG

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95/10/19	20-625:951019	MMD Sub	Clinical		RESPONSE TO FDA REQ: 8 VOLS/ RESPONSE TO REQUEST BY GUS TRUHER 10/13/95 - 8 VOLS RE: PROTOCOLS PJPR0009, 010, 023, 024, 003, 007. LJG
	20-625:951019A	FDA Tel	Clinical		CONTACT:BBONO/SAK:PJPR0007/ECG/ BARBARA BONO CALLED SALLY KORTY RE: QUESTIONS ABOUT ECG DATA ON PJPR0007. AEF
95/10/23	20-625:951023	FDA Tel	Clinical		CONTACT:KLEE/CKY:QUESTIONS/ KOUNG LEE, ALONG WITH DR. SEVKA AND DR. BONO PHONED CINDY REGARDING A QUESTION ON DATA IN THE SUBMISSION. AEF
95/10/24	20-625:951024	MMD Ltr	ALL		CKY/KLEE: REQUEST FOR MEETING/ REQUEST A 90 DAY CONFERENCE TO DETERMINE STATUS OF REVIEW OF APPLICATION.
95/10/26	20-625:951026	MMD Tel	Clinical		CONTACT:CKY/KLEE:TELECON/ MMD INITIATED A TELECON WITH THE FDA. AEF
	20-625:951026A	FDA Tel	Clinical		CONTACT:KLEE/CKY:TELECON/ KLEE TELEPHONED TO SEE IF WE COULD PROVIDE A DESCRIPTION OF THE MATERIALS RDW RETAINED AT THIER SITE. AEF
95/11/01	20-625:951101	MMD Ltr	Clinical		RESPONSE TO FDA REQ: DESK COPY/ REF: DR SEVKA'S REQUEST 10/26/95 - CONVERSION OF PROTOCOLS PJPR003 & 007 TO WORDPERFECT 6.0A. LJG
	20-625:951101A	FDA Tel	Other		CONTACT:BBONO/BAHLBRANDT:CAT/ BARBARA BONO CALLED BOB AHLBRANDT RE: CAT LISTINGS. AEF
95/11/02	20-625:951102	MMD Ltr	Clinical		AMENDMENT TO RESP TO FDA REQ/ PJPR0003 SINGLE PAGE FOR PATIENTS 31 AND 32 FROM APPENDIX C.4.A.1. LISTING FOR INSERTION IN SECTIONS 6 AND 8. LJG

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FEXOFENADINE HYDROCH
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95/11/02	20-625:951102A	FDA Tel	Clinical		CONTACT:BGILLESPIE/TRUSSELL:FE/ BRAD GILLESPIE CALLED TANYA RUSSELL TO FIND OUT IF ANY IN VITRO WORK HAD BEEN DONE WITH THIS PRODUCT. AEF
	20-625:951102B	MMD Fax	Biopharm		FAX:TR/BGILLESPIE:BIOPHARM/ TANYA RUSSELL FAXED BRAD A COPY OF A PAGE FROM REPORT K-94-0869-D AS HE REQUESTED FROM CINDY KIRK-YOURTEE. AEF
95/11/06	20-625:951106	FDA Tel	Biopharm		CONTACT:BBONO/BA:RESULTS/ BARBARA BONO CALLED BOB AHLBRANDT TO SEEK CONFIRMATION ON THE RESULTS ON A TABLE ON PAGE 89 OF THE NDA. AEF
	20-625:951106A	FDA Tel	Biopharm Clinical		CONTACT:KLEE/CKY:REQUEST 90 DY/ KOUNG LEE CALLED TO RESPOND TO CKY'S REQUEST FOR A 90 DAY CONFERENCE RE: STATUS OF THE APPLICATION. AEF
	20-625:951106B	FDA Mtg	GMP		NOVEMBER 6, 1995 FDA INSPECT./ DAY 1 OF FDA INSPECTION.
95/11/13	20-625:951113	MMD Tel	ADR Clinical		CONTACT:CKY/KLEE:ADR REPORTS/ CINDY CONTACTED KOUNG LEE TO ADVISE HIM OF THE 100+ 15 ADR REPORTS THAT WERE COMING. ALSO DISCUSSED WERE FEXO NDA AND FEXO-D. AEF
	20-625:951113A	MMD Tel	GMP		CONTACT:RRL/KRODEN:INSPECT/ AN INSPECTION TO SEE SUMMARY REPORTS ON WATER CHEMICAL AND MICRO TEST RESULTS WAS CONDUCTED. AEF
95/11/14	20-625:951114	MMD Tel	GMP		CONTACT:RRL/KRODEN:INSPECT/ INSPECTION TOOK PLACE THIS SHOULD RUN THROUGH 11/22/95. AEF
	20-625:951114A	MMD Mtg	GMP		CONTACT:RRL/DBERGESSON:INSPECT/ INSPECTION OF MARS SYSTEM TOOK PLACE BY THE FDA. AEF
95/11/15	20-625:951115	MMD Tel	Other		CONTACT:RRL/KRODEN:INSPECT/ A GENERAL INSPECTION OCCURRED TODAY FOR CONTINUATION OF REVIEW BY FDA. AEF
95/11/16	20-625:951116	FDA Tel	Clinical		CONTACT:BGILLESPIE/CKY:REQUEST/ BRAD GILLESPIE CALLED CINDY TO REQUEST AN IN VITRO REPORT AND PJPR0021. AEF

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95 11 16	20-625:951116A	FDA Tel	ADR Clinical		CONTACT:CKY/KLEE:ADVISE/ CINDY CALLED KOUNG TO INFORM HIM OF THE TEAM'S MEETING TO RETRACT URTICARIA AND FEX-D MEETING REQUEST. KOUNG SAID WHEELS WERE TURNING AND HIS WARNING WAS FOR FUTURE SUBMISSIONS. AEF
	20-625:951116B	MMD Tel	Other		COPY OF DATA FROM 48,486:951116 CONTACT:RRL/KRODEN:INSPECT/ GENERAL INSPECTION CONTINUED. AEF
95 11 17	20-625:951117	MMD Ltr	Other		RESPONSE TO FDA REQ:10/27 MINU/ SUMMARY OF MINUTES OF 10/27/95 TELECON- FERENCE AS REQUESTED BY KOUNG LEE. LJG
	20-625:951117A	FDA Tel	Clinical		CONTACT:GSTRANGE/CKY:PJPR0019/ GRETCHEN STRANGED CALLED TO REQUEST A COPY OF THE DIARY PAGE FOR PJPR0039. AEF
	20-625:951117B	FDA Tel	Clinical		CONTACT:KLEE/CKY:DIARY/ KOUNG LEE TELEPHONED TO INFORM CINDY THAT THE REQUEST FOR THE DIARY WAS FOR THE COMPLETE DIARY NOT A PAGE AS PREVIOU SLY REQUESTED. AEF
95 11 20	20-625:951120	MMD Sub	Clinical		LTR:CKY/KLEE:PROTOCOLSY CINDY SENT KOUNG COPY OF PJPR0021 AND K-95-0137-D AT BRAD GILLESPIE'S REQUEST. AEF
	20-625:951120A	MMD Tel	Clinical Other		CONTACT:CKY/KLEE:PJPR0021/ CINDY CALLED KOUNG TO INFORM HIM THAT HIS REQUEST FOR PJPR0021 WAS COMING THIS WEEK. ALSO DISCUSSED WAS SELDANE/ FEX MEETINGS. AEF
	20-625:951120B	MMD Tel	Other		CONTACT:RRL/KRODEN:INSPECT/ AN INSPECTION TOOK PLACE TO RESUME FROM THE DAY BEFORE. AEF
95 11 21	20-625:951121	FDA Tel	Other		CONTACT:RLOHREY/KRODEN:INSPECT/ AN FDA INSPECTION TOOK PLACE TODAY WITH THE FDA. AEF

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95/11/22	20-625:951122	MMD Fax	Clinical		FAX:CKY/KLEE:PATIENT DIARY/ CINDY SENT KOUNG LEE A FAX PER HIS REQUEST FOR PATIENT DIARIES FOR PJPR0039 PJPR0019 WAS SENT SINCE PJPR0039 HAS NO DIARY. AEF
	20-625:951122A	MMD Tel	Other		CONTACT:RLOHREY/KRODEN/INSPECT/ RICK LOHREY HAD FDA TOURING FOR THE 12TH DAY FOR INSPECTIONS. AEF
95/11/27	20-625:951127	FDA Tel	Clinical Other		CONTACT:KLEE/CKY:PROPOSAL/ KOUNG CALLED CINDY TO INFORM HER THAT DRS SEVKA, HIMMEL, O'CONNOR & GILLESPIE MET TO DISCUSS DEVELOPMENT PLAN. SELDANE AND FEX-D WERE ALSO DISUSSED. AEF
95/11/30	20-625:951130	MMD Sub	Other		LTR:CKY/FDA:FOUR MONTH UPDATE/ CINDY SENT LETTER TO FDA RE: 4 MONTH SAFETY UPDATE ON FEXOFENADINE. AEF
	20-625:951130A	FDA Mtg	GMP		GMP INSPECTION/ THE INVESTIGATORS COLLECTED SAMPLES FOR THEIR INSPECTION OF VARIOUS PRODUCTS. CALIBRATION WAS COVERED. LOOKED AT NEW CIP SYSTEM, ETC.
95/12/01	20-625:951201	FDA Mtg	GMP		FEXOFENADINE PRE-APPROVAL INSP/ GENERAL GMP AND FEXOFENADINE PRE-APPROVAL INSPECTION.
95/12/04	20-625:951204	FDA Tel	Clinical		CONTACT:MSEVKA/CKY:ANALYSES/ SEVKA PHONED TO REQUEST HELP WITH ADDITIONAL ANALYSES. AEF
	20-625:951204A	FDA Mtg	GMP		FEXOFENADINE PRE-APPROVAL INSP/ GENERAL GMP INSPECTION AND FEXOFENADINE PRE-APPROVAL INSPECTION. FINISH DITROPAN AND PAVABID VALIDATION TODAY.
95/12/08	20-625:951208	MMD Sub	Clinical		LTR:CKY/KLEE:RESPONSE/ RESPONSE TO FDA REQUEST. DR SEVKA'S QUESTIONS OF 12/4/95. AEF

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95/12/08	20-625:951208A	MMD Ltr	GMP		FDA 483/ 483 ISSUED 12/8/95 THAT INCLUDED 15 OBSERVATIONS. 1-6 ASSOCIATED W/PEXOFENADINE, 7-11 ASSOCIATED W/MARS, 12&13 CARDIZEM CD AND 14 AND 15 GENERAL GMP.
95/12/11	20-625:951211	MMD Tel	Clinical Other		CONTACT:CKY/MS/KLEE:PANEL/ CKY HAD TELECON WITH MIKE SEVKA AND KOUNG LEE RE: PANEL FOR PEXOFENADINE. SELDANE/SELDANE-D, SELDANE IND AND NDL 16,455A WERE ALSO DISCUSSED. AEF
95/12/13	20-625:951213	MMD Sub	Clinical		RESPONSE TO FDA REQUEST/ REFERENCE TO DR SEVKA'S REQUEST OF 12/11/95. RESPONSE TO 4 QUESTIONS. LJG
95/12/15	20-625:951215	FDA Tel	Clinical		CONTACT:MSEVKA/CKY:REQUEST/ DR. SEVKA TELEPHONED TO INFORM CINDY THAT HE RECEIVED OUR 12/13 TO HIS 12/11 QUESTIONS. HE NOW HAD SEVERAL MORE REQUESTS. AEF
95/12/18	20-625:951218	FDA Ltr	GMP		RESPONSE TO 483 ISSUED 12/8/95/ RESPONSE TO 15 FDA 483 OBSERVATIONS.
95/12/21	20-625:951221	MMD Sub	Clinical		LTR:CKY/KLEE:RESPONSE/ CINDY SENT LETTER - RESPONSE TO DR. SEVKA'S REQUEST OF 12/15 FOR ECG'S FROM PJPR0007 HANDLING TECHNIQUES. AEF
95/12/22	20-625:951222	MMD Sub	Clinical		REPONSE TO REQUEST/ RESPONSE TO SEVKA'S REQUEST OF 12/15/95. (KAL)
96/01/16	20-625:960116	FDA Tel	Other		CONTACT:KLEE/CKY:PANEL DATES/ KOUNG LEE LEFT MESSAGE THAT MAY 9-10 WERE DATES FOR PANEL. AEF

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96/01/17	20-625:960117	MMD Tel	Clinical		CONTACT:CKY/MSEVKA:MEETING/ A TELECON WITH CINDY AND BOB AHLBRANDT (MMR), STEVE WILSON, BARBARA BONO, KOUNG LEE, AND MIKE SEVKA (FDA) WAS REQUESTED TO DISCUSS RECENT FINDINGS FROM AN FDA AUDITOR AT SITE PJPR0009/PST0021. AEF
96/01/19	20-625:960119	MMD Sub	Clinical		FAX:CKY/KLEE:SUMMARY OF DISCUS/ CINDY SENT FAX TO SEKVA REGARDING THE DISCUSSION OF 1/18/96. AEF
	20-625:960119A	MMD Sub	Clinical		LTR:CKY/KLEE:AMENDMENT/ CINDY SENT LETTER TO KOUNG LEE RE: AMENDMENT TO FDA RESPONSE TO PJPR0009. AEF
	20-625:960119B	MMD Fax	Clinical		FAX:CKY/MSEVKA:SUMMARY OF MTG/ CINDY SENT FAX TO MIKE SEVKA RE: SUMMARY OF MEETING. AEF
	20-625:960119C	MMD Tel	Clinical		CONTACT:CKY/MSEVKA:REVISED PRO/ CINDY CONTACTED MIKE SEVKA TO INDICATE THAT A REVISED CSR FOR PJPR0009 COULD BE AVAILABLE WITHIN THE FIRST 2 WEEKS OF FEBRUARY, BOB AHLBRANDT ALSO WAS IN ATTENDANCE. AEF
96/01/22	20-625:960122	FDA Tel	Clinical		CONTACT:BBONO/BA:PJPR0010/ BARBARA BONO CALLED BOB AHLBRANDT TO AS TWO QUESTIONS ON PJPR0010. AEF
96/01/24	20-625:960124	FDA Tel	Clinical		CONTACT:BBONO/BA:QUESTIONS/ BOB AHLBRANDT RECEIVED CALL FROM BARBARA BONO RE: TWO QUESTIONS ON PJPR0010 REPORT. AEF
	20-625:960124A	MMD Fax	Clinical		FAX:CKY/MSEVKA:LISTINGS/ CINDY FAXED MIKE SEVKA COPIES OF LISTINGS AS HE REQUSTED FOR PJ0R0009, 0010, 0023, 0024. AEF

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FEXOFENADINE HYDROCH
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Submission Date	Log Number IND/NDA:Date	Origin/ Type	Classi- fication	Supp/ Serial#	Description/ Comments
96/01/24	20-625:960124B	FDA Tel	Clinical		CONTACT:MSEVKA/CKY:MEETING/ SEVKA PHONED RE; INTERNAL FDA MEETING TO DISCUSS FDA RECOMMENDATIONS FOR RECONCILATIONS OF ERRONEOUS TREATMENT ASSIGNMENTS FOR PJPR0009. AEF
96/01/26	20-625:960126	MMD Sub	Clinical		RESPONSE TO SEVKA REQUEST/ REFERENCE TO DR. SEVKA'S REQUEST OF 1/24/96 FOR LISTINGS OF PATIENTS IN PJPR0009, PJHPR0010, PJPR0023 AND PJPR0024 WHO WERE RANDOMIZED, BUT NOT INCLUDED IN THE INTENT-TO-TREAT ANALYSIS LJG
96/01/30	20-625:960130	MMD Ltr	Other		AUTHORIZE FDA DISCLOSE INFO./ TO AUTHORIZE FDA TO DISCLOSE INFORMATION FROM NDA TO DRUGS DIRECTORATE OF THE HEALTH PROTECTION BRANCH, MINISTRY OF HEALTH, CANADA (HPB). LJG
96/01/31	20-625:960131	FDA Tel	Clinical		CONTACT:MSEVKA/CKY:VERIFICATIO/ MIKE SEVKA CALLED REQUESTING VERIFICATION (IN WRITING) OF OBSERVATIONS. AEF
96/02/02	20-625:960202	MMD Tel	Clinical Other		CONTACT:CKY/MSEVKA:PANEL DATES/ CINDY CONTACTED MIKE SEVKA TO FOLLOW-UP ON REQUESTS HE INDICATED WOULD BE COMING THIS WEEK. AEF
96/02/05	20-625:960205	FDA Tel	Other		CONTACT:KLEE/CKY:CLARIFICATION/ KOUNG LEE RETURNED CINDY'S CALL RE: HER REQUEST FOR CLARIFICATION OF PANEL DATES. AEF

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96/02/08	20-625:960208	FDA Tel	Biopharm CMC		CONTACT:KLEE/CKY:CHANGES/ KOUNG LEE TELEPHONED TO INFORM CINDY THAT HE IS LEAVING THE FDA AND THAT GRETCHEN STRANGE WOULD BE TAKING HIS PLACE FOR ALLEGRA. AEF
96/02/09	20-625:960209	NMD Fax	Clinical		FAX:CKY/MSEVKA/STRANGE:PJPR9/ CINDY FAXED GRETCHEN STRANGE/MICHAEL SEVKA A COPY OF THE PJPR0009 AMENDMENT TO 1/19/96 SUBMISSION TO INFORM HER THAT IF WILL OFFICIALLY SUBMITTED. AEF
	20-625:960209A	NMD Sub	Clinical		RESPONSE TO FDA REQ: ECG RHYTH/ RESPONSE TO FDA REQUEST OF 1/19/96 - ECG RHYTHM STRIPS FOR TEN SUBJECTS/ PATIENTS WITH MAXIMUM PLASMA CONCENTRA- TIONS IN STUDIES PJPR0003, PJPR0007, PJPR0023, PJPR0024 AND PJPR0018, PJPR0028. LJG
96/02/12	20-625:960212	NMD Sub	Clinical		RESPONSE TO FDA REQ: PJPR0009/ REFERENCE TO DISCUSSION OF 1/31/96 REQUEST ADDITIONAL INFORMATION RE: TREATMENT ASSIGNMENTS IN PROTOCOL PJPR0009. LJG
	20-625:960212A	FDA Tel	CMC		CONTACT:CBERTHA/CKY:CMC/ CRAIG BERTHA CALLED CINDY TO EXPLAIN THAT HE WAS JUST ASSIGNED TO THE CMC SECTION OF THE ALLEGRA NDA. AEF
96/02/13	20-625:960213	NMD Tel	CMC		CONTACT:PM/CBERTHA:SUMMARY/ PHIL MISCHLER HAD TELECON WITH CRAIG BERTHA AND G POOCHIKIAN RE: THE STABILITY PROTOCOL FOR COMMERCIAL PRODUCTS LOTS. AEF

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96/02/13	20-625:960213A	FDA Tel	Clinical		CONTACT:MSEVKA/CKY:TABLES/ MIKE SEVKA CALLED TO REQUEST IF WE CAN CREATE TABLES TO REPRESENT ANALYSES OF AGE GENDER AND RACE ACROSS 4 ADEQUATE AND WELL CONTROLLED TRIALS. AEF
96/02/14	20-625:960214	FDA Fax	Clinical		FAX:PH/CBERTHA:SUMMARY PROT/ PHIL MISCHLER FAXED CRAIG BERTHA RE: SUMMARY OF STABILITY PROTOCOL. AEF
96/02/15	20-625:960215	MMD Sub	CMC		CMC AMENDMENT:STABILITY/STATIS/ CMC AMENDMENT PROVIDING ADDITIONAL STABILITY DATA ALONG WITH STATISTICAL ANALYSIS AND RESPONSE TO AN INFORMAL QUESTION ASKED BY THE REVIEWING CHEMIST REGARDING ABILITY OF HYDRATED FORM OF DRUG SUBSTANCE TO REVERT BACK TO ANHYDROUS FORM IN GRANULATIONS STORED AT LOWER HUMIDITY. LJG
	20-625:960215A	MMD Mtg	CMC		TAM STABILITY, GAVS-2 SUPPLMNT/ CONTACT: DSHAH/GPOOCHIKIAN, JGIBBS, RWOLTERS: GENERAL DISCUSSIONS ON TAM, CARDIZEM LYO-JECT, GAVISCON TABS.
96/02/16	20-625:960216	FDA Tel	Biopharm		CONTACT:BGILLESPIE/CKY:REQUEST/ BRAD GILLESPIE PHONED TO REQUEST INFO ON DISSOLUTION DATA. AEF
96/02/21	20-625:960221	MMD Sub	Clinical		RESPONSE TO FDA REQ. OF 2/2/96/ RESPONSE TO FDA REQUEST OF 2/2/96 RE: PJPR0009 AND PJPR0010. LJG
	20-625:960221A	FDA Tel	Biopharm		CONTACT:BGILLESPIE/CKY:LOTS/ BRAD GILLESPIE CALLED TO CONFIRM THAT THE LOTS HE REQUESTED ON 2/16/96 WERE "RG" NOT "RB". AEF
	20-625:960221B	MMD Fax	Biopharm		FAX:CKY/BGILLESPIE:REQUEST/ CINDY SENT FAX AT BRAD'S REQUEST OF 2/16/96 FOR LOT NUMBERS. AEF

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96/02/22	20-625:960222	MMD Tel	Biopharm		FAX:CKY/BGILLESPIE:VOICEMAIL/ CINDY SENT FAX TO BRAD RE: RECEIVING HER VOICE MAIL RE: THE SERIES OF RG LOT NUMBERS PROVIDED ON 2/21/96. AEF
	20-625:960222A	MMD Fax	Clinical		FAX:CKY/MSEVKA:TABLES/ CINDY FAXED FORMAT FOR TABLES THAT SEVKA REQUESTED 2/13/96. AEF
96/02/23	20-625:960223	MMD Ltr	CMC		LTR:DNS/GPOOCHIKIAN/DRAFT PROT/ LTR:SENT VIA FAX TO GPOOCHIKIAN BY DNS. CHEMISTRY, MANUFACTURING & CONTROL (CMC) DRAFT STABILITY PROTOCOL FOR DR BERTHA AND DR POOCHIKIAN REVIEW.
96/02/26	20-625:960226	FDA Tel	Clinical		CONTACT:BBONO/BA:PJPR0007/ BARBARA BONO CALLED BOB AHLBRANDT RE: REVIEWING QTC ANALYSES IN PJPR0007. AEF
	20-625:960226A	MMD Fax	Clinical		FAX:BA/BBONO:SAS VARIABLES/ BOB AHLBRANDT SENT FAX TO BARBARA BONO FOR PROGRAMMING SAS USED TO CREATE LOG VARIABLE FOR PJPR0007 QTC ANALYSIS. AEF
96/02/27	20-625:960227	MMD Fax	Clinical		LTR:CKY/MSEVKA:RESPONSE/ CINDY FAXED LETTER TO MIKE SEVKA RE: SUBMISSION OF 2/21/96 WHERE SENTENCE WAS LEFT OUT. AEF
	20-625:960227A	MMD Ltr	Clinical		OMITTED SENTENCE TO 2/21 RESP/ IN THE FEBRUARY 21 RESPONSE ONE SENTENCE WAS INADVERTENTLY OMITTED FROM SECOND PARAGRAPH RE: PK QUESTION. LJG
	20-625:960227B	MMD Fax	Clinical		FAX:BA/BBONO:SAS TABLES/ BOB AHLBRANDT SENT FAX TO BARBARA BONO RE: SAS PROGRAM COSE AND SAS OUTPUT USED TO EXPLORE THE BASELINE BY TREATMENT INTERACTION IN PJPR0010. AEF

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96/02/27	20-625:960227C	FDA Tel	Clinical		CONTACT:BBOHO/BA:PJPR0010/ BARBARA BOHO AND BOB AHLBRANDT HAD PHONE CONVERSATIONS ON 2/26 AND 2/27 ON PJPR0010. AEF
96/03/01	20-625:960301	FDA Tel	Clinical		CONTACT:MSEVKA/CKY:TELEMETRY/ SEVKA CALLED RE: TELEMETRY DATA. CINDY EXPLAINED THEY WERE NOT RECORDED. AEF
	20-625:960301A	NMD Sub	CMC		RESPONSE TO REQUEST/ DRAFT COPY OF STABILITY PROTOCOL FOR REVIEW BY DR. POOCHIKIAN AND BERTHA. (KAL)
	20-625:960301B	NMD Tel	CMC Drug-Master		DMF ACCESS LETTER/ CONTACT: DSHAH/CBERTHA: DISCUSS DMF ACCESS LETTERS.
	20-625:960301C	FDA Tel	Clinical		CONTACT:MSEVKA/CKY:PJPR0003/ MIKE SEVKA PHONED TO REQUEST EXPLANATION FOR CHANGES OBSERVED IN BICARB/CHLORIDE LAB VALUES FOR PJPR0003. AEF
96/03/04	20-625:960304	NMD Sub	Clinical		DISKETTE F012996.WIN WP6.1/ RESPONSE TO FDA REQUEST RE: TABLES SUPPORTING DEMOGRAPHIC ANALYSIS OF DATA PREVIOUSLY SUBMITTED - INFO SUBMITTED IN FILE F021996.WIN IN WORDPERFECT 6.1. LJG
	20-625:960304A	NMD Fax	Clinical		FAX:CKY/MSEVKA:ECG DATA/ CINDY FAXED MIKE SEVKA RE: DESCRIPTION OF HOW ECGS DATA WERE COLLECTED AND DAILY MEANS COMPUTED IN PJPR0003, 4, 7, 18 AND 28.
96/03/06	20-625:960306	FDA Tel	Clinical		CONTACT:CKY/MSEVKA/STRANGE:REQ/ MIKE SEVKA AND GRETCHEN PHONED CINDY WITH A SERIES OF REQUESTS. AEF

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96/03/11	20-625:960311	FDA Tel	Other		CONTACT:GSTRANGE/PH:QUESTION/ GRETCHEN STRANGE CALLED FOR CINDY, I TRANSFERRED TO PAUL NEIHOUSE. SHE WANTED TO KNOW WHERE ELSE FEXO WAS GOING SUBMITTED BY 7/31/96, SHE ALSO STATED THAT WE CANNOT USE THE TRADENAME ALLEGRA.. AEF
	20-625:960311A	MMD Tel	Other		CONTACT:PFH/GSTRANGE:RESPONSE/ PAUL NEIHOUSE CALLED GRETCHEN BACK PER HER CALL EARLIER IN THE DAY RE: TRADENAME FOR ALLEGRA. AEF
	20-625:960311B	FDA Tel	CMC		CONTACT:CBERTHA/PFH:CMC SECT/ CRAIG BERTHA CALLED WITH QUESTIONS ON THE CMC SECTION (PACKAGING). AEF
	20-625:960311C	FDA Tel	CMC		CMC PACKAGING ISSUES/ CONTACT: DSHAH/CBERTHA: CMC PACKAGING ISSUES ON THE NDA.
96/03/12	20-625:960312	FDA Tel	Clinical		CONTACT:MSEVKA/PFH:QUESTION/ MIKE SEVKA CALLED PAUL FOR ADDITIONAL QUESTIONS ON POLLEN COUNTS FOR PJPR0009, 10, 23 AND 24. AEF
	20-625:960312A	FDA Tel	Clinical		CONTACT:MSEVKA/PFH:INFOR/ MIKE SEVKA CALLED FOR AN ADDITIONAL PIECE OF INFORMATION ON OUR 3/6/96 SUBMISSION. AEF
96/03/13	20-625:960313	FDA Tel	Clinical		CONTACT:MSEVKA/PFH:PJPR0007/ MIKE SEVKA CALLED WITH ADDITIONAL QUESTIONS ON PJPR0007. AEF
	20-625:960313A	MMD Tel	Other		CONTACT:PFH/GSTRANGE:MISC/ PAUL CONTACTED GRETCHEN STRANGE ON THE NAME ALLEGRON. WE ARE NOT ABLE TO USE OUR TRADENAME ALLEGRA BECAUSE OF THE CLOSE SIMILARITY TO THIS NAME. AEF
	20-625:960313B	FDA Tel	Clinical		CONTACT:MSEVKA/PFH:QUESTIONS/ QUESTIONS ASKED BY SEVKA ON PJPR0007. AEF
96/03/14	20-625:960314	FDA Tel	Clinical		CONTACT:GSTRANGE/PFH:REQUEST/ GRETCHEN CALLED TO REQUEST ADDITIONAL COPY OF A VOLUME 8.1. AEF

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96/03/15	20-625:960315	FDA Tel	Other		CONTACT:GSTRANGE/CKY:NO PANEL/ GRETCHEN CALLED TO INFORM CINDY THAT THE MAY 9-10 PANEL IS CANCELLED. AEF
	20-625:960315A	FDA Tel	Clinical Other		CONTACT:MSEVKA/CKY:PANEL/ MIKE SEVKA AND GRETCHEN CALLED FOLLOWING GRETCHEN'S CALL REGARDING PANEL. SEVKA HAS MORE QUESTIONS ON NDA. AEF
96/03/18	20-625:960318	FDA Tel	Clinical		CONTACT:BBONO/BA:PJPR0007/ BOB RECEIVED MESSAGE FROM BARBARA BONO ON PJPR0007 ECG DATA. AEF
	20-625:960318A	MMD Tel	Other		CONTACT:PFH/MSEVKA:PANEL/ PAUL CALLED MIKE SEVKA TO VERIFY THAT THE FEXOFENADINE ADVISORY PANEL MEETING WAS CANCELLED. AEF
96/03/20	20-625:960320	FDA Tel	Clinical		CONTACT:MSEVKA/PFH:MORE QUESTS/ MIKE SEVKA CALLED WITH ANOTHER REQUEST. THESE WERE FOR PJPR0004 AND A FOLLOW-UP TO PJPR0003. AEF
	20-625:960320A	MMD Tel	Other		CONTACT:PFH/GSTRANGE:NAME/ GSTRANGE STATED THAT IF WE CAN PROVIDE IN WRITING OUR REASONING FOR USE OF THE NAME ALLEGRA BY 3/26 SHE WILL TAKE TO NOMENCLATURE COMMITTEE. AEF
96/03/22	20-625:960322	MMD Fax	Other		TRADENAME JUSTIFICACTION LTR./ FAXED COPY TO GSTRANGE - ALLEGRA TRADENAME JUSTTIFICATION LETTER. LJG
	20-625:960322A	MMD Ltr	Other		LTR: TRADENAME JUSTIFICATION/ LETTER FOR ALLEGRA TRADENAME JUSTIFICATION. LJG
	20-625:960322B	MMD Mtg	Other		CONTACT:PFH/GSTRANGE:LETTER/ PAUL INFORMED GRETCHEN THAT HE WAS IN THE PROCESS OF FAXING HER THE LETTER RE: REASONS WHY MMR BELIEVES WE SHOULD BE ALLOWED TO USE THE TRADENAME. AEF

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96/03/25	20-625:960325	MMD Ltr	Clinical		RESPONSE TO FDA REQUEST/ REF. TO DR SEVKA'S REQUEST OF 3/12/96 RE: 4 PIVOTAL TRIALS PJPR0009, 010, 023, 024 - UNIT OF MEASURE FOR POLLEN COUNTS. LJG
96/03/26	20-625:960326	FDA Tel	Clinical		PHONE:GSTRANGE/CKY/WRONG DATES/ PHONE:GCSTRANGE/CKY/INFORMED THAT THE NOMENCLATURE COMMITTEE HAD GIVEN HER THE WRONG DATE. IT WILL BE HELD ON APRIL 16, 1996.
	20-625:960326A	MMD Tel	CMC	026	CONTACT:RLOHREY/MGARZA:INSPECT/ RE: EER (ESTABLISHMENT EVALUATION REPORT BEING SENT TO KC DISTRICT FOR S-026 DITROPAN. RLOHREY ALSO INFORMED GARZA THAT PROCESS VALIDATION FOR MFG OF FEXOFENADINE CAPSULRES WAS NEARLY COMPLETE. LJG COPY OF DATA FROM 17-577:960326
96/04/01	20-625:960401	MMD Sub	Clinical		RESPONSE TO FDA REQUEST/ REFERENCE TO FDA REQUEST OF 3/6, 3/13, 3/15, & 3/20/96 ASSOCIATED WITH PJPR0003, PJPR0004, PJPR0007, PJPR0010, PJPR0018, PJPR0023, PJPR0024 AND PJPR0028. LJG
96/04/02	20-625:960402	MMD Tel	CMC		DMF PACKAGING COMPONENTS/ CONTACT: DSHAH/CBERTHA: FOLLOW-UP ON ISSUES RAISED ON SEVERAL DMFS FOR PACKAGING COMPONENTS.
96/04/09	20-625:960409	MMD Tel	CMC		DRUG PLAST DMF ISSUE/ CONTACT: DSHAH/CBERTHA: FOLLOW UP ON DRUG PLASTIC DMF ISSUE.

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96/04/12	20-625:960412	NMD Sub	CMC		CMC AMENDMENT/ NOITIFY AGENCY THAT DRUG PLASTIC AND GLASS CO WILL SUPPLY ON THE THE GAL. SZ. HDPE BOTTLES FOR PACKAGING. (KAL)
	20-625:960412A	NMD Tel	Clinical		PHONE:CKY/MSEVKA/COPY OF RPT/ PHONE CONTACT:CKY/MSEVKA/WE WOULD BE PROVIDING HIM A COPY OF CANADIAN RABBIT REPORT.
	20-625:960412B	NMD Fax	Other		FAX:CKY/GSTRANGE TRADENAME QUE/ FAX TO GSTRANGE REQUESTING NONMENCLATURE COMMITTEE TO ADDRESS SEVERAL QUESTIONS REGARDING THE TRADENAME ALLEGRA. KML
	20-625:960412C	NMD Sub	Other		SUBMISSION OF 4/12 FAX/ SUBMISSION OF 4/12 FAX REQUESTING NOMMENCLATURE COMMITTEE TO ADDRESS SEVERAL QUESTIONS REGARDING TRADENAME ALLEGRA. KML
96/04/16	20-625:960416	NMD Tel	Other		PHONE:CKY/GSTRANGE/UPDATE PROG/ PHONE: CKY/GSTRANGE/TO OBTAIN AN UPDATE ON PROGRESS AND DETERMINE STATUS OF THE NOMENCLATURE COMMITTEE ACTIVITY. COPY OF DATA FROM 18-949:960416
96/04/17	20-625:960417	NMD Sub	Pre-Clin		SUBMISSION:RESPONSE TO REQUEST/ SUBMISSION OF DRAFT REPORT OF CANADIAN STUDY IN RABBITS WERE FEXOFENADINE AND TERFENADINE WERE EXAMINED IN RESPONSE TO REQUEST. KML
96/04/18	20-625:960418	FDA Ltr	CMC		LTR:JJENKINS/CKY:CMC QUESTIONS/ THIS IS LETTER OF FAX THAT CAME VIA FAX ON 4/23/96 RE: FDA REVIEW OF CMC SECTION FOR THIS NDA. AEF

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96/04/18	20-625:960418A	FDA Mtg	Clinical Other		CONTACT:MSEVKA/CKY:EDUC PACK/ CINDY MET WITH DR. SEVKA TO PROVIDE HIM AND OVERVIEW OF THE EDUCATIONAL PACKAGE FOR SELDANE.
96/04/19	20-625:960419	FDA Tel	Clinical Other		CONTACT:MSEVKA/AEF:REQUESTS/ SEVKA CALLED FOR CINDY AND ANGELIQUE TOOK THE MESSAGE. SEVKA HAD SEVERAL REQUESTS THAT HE NEEDED BY THE END OF THE DAY OF APRIL 22, 1996. AEF
96/04/22	20-625:960422	MMD Fax	Other		FAX:CKY/GSTRANGE:MEETING/ CINDY FAXED GRETCHEN STRANGE LETTER FOR REQUEST FOR 24-HOUR EMERGENCY MEETING WITH THE NOMENCLATURE COMMITTEE RE: TRADEMARK FOR ALLEGRA. AEF
	20-625:960422A	MMD Fax	Other		FAX:CKY/MSEVKA:REQUEST/ CINDY FAXED MIKE SEVKA INFORMATION HE REQUESTED ON 4/19 RE: DEAR DOCTOR LETTERS THAT WERE SUBMITTED IN 1992. CKY PULLED 12/5/95 LTR FOR SAME SUBJECT. AEF
	20-625:960422B	MMD Ltr	Other		REQ. FOR 24-HR EMERGENCY MTG/ REQUEST A 24-HR EMERGENCY PROCEDURE CONSULT WITH NOMENCLATURE COMMITTEE TO DETERMINE THE ACCEPTABILITY OF TRADEMARK FOR FEXOFENADINE HCL, ALLEGRA. LJG
	20-625:960422C	MMD Fax	Clinical		FAX:CKY/MSEVKA:RESP TO REQ/ CINDY SENT FAX OF SUBMISSION THAT WAS GOING OUT TONIGHT VIA FEDEX RE: RESPONSE TO SEVKA'S REQUEST NEEDED BY END OF 4/22. AEF
96/04/23	20-625:960423	MMD Sub	Clinical		LTR:CKY/MSEVKA:RESP TO REQ/ CINDY SENT LETTER TO SEVKA RE: RESPONSE TO REQUEST THAT SEVKA NEEDED BY 4/22. EVEN THOUGH IT WAS SENT 4/22 AND LETTER IS DATED 4/23. FAX OF THIS SUBMISSION WAS ALSO SENT BY FAX ON 4/22. AEF

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96/04/23	20-625:960423A	FDA Fax	CMC		FAX:GSTRANGE/CKY:CMC RESPONSE/ FDA HAS COMPLETED REVIEW OF THE CMC SECTION FOR THIS NDA AND HAS THE FOLLOWING COMMENTS (SEE FAX). AEF
	20-625:960423B	MMD Tel	CMC		SECONDARY PACKAGING/ CONTACT: DSHAH/CBERTHA AND GSTRANGE: DISCUSS PROPOSAL OF SECONDARY PACKAGING.
96/04/24	20-625:960424	MMD Tel	Biopharm Clinical		CONTACT:WS/BBONO:ECGS/ WILL SULLIVAN CALLED BARBARA BONO RE: ECGS FROM PROTOCOL PJPR0007. AEF
96/04/25	20-625:960425	FDA Tel	Clinical Other		CONTACT:MSEVKA/CKY:REQUESTS/ SEVKA CALLED WITH ADDITONAL REQUESTS FROM CINDY. AEF
	20-625:960425A	FDA Tel	Other		CONTACT:GSTRANGE/CKY:TRADENAME/ GRETCHEN CALLED TO INFORM CINDY THAT THE FDA HAS REVERSED THEIR DECISION RE: THE TRADEMARK FOR ALLEGRA. AEF
	20-625:960425B	MMD Tel	CMC		CLARIFICATION & GUIDANCE/ CONTACT: DSHAH/CBERTHA AND BROGERS: SEEK CLARIFICATION AND GUIDANCE ON SOME OF THE QUESTIONS.
	20-625:960425C	MMD Tel	CMC		CONTACT:CKY/GSTRANGE:CMC ISSUE/ CINDY PHONED GRETCHEN STRANGE REGARDING A CONVERSATION THAT DHIREN SHAH HAS WITH THE CHEMISTRY REVIEWERS FOR THE DIVISION. AEF
96/04/26	20-625:960426	FDA Tel	Biopharm Clinical		CONTACT:MSEVKA/CKY:ISS/ISE/ SEVKA CALLED WITH ADDITIONAL QUESTIONS ON THE SUBMISSION. AEF
	20-625:960426A	MMD Sub	CMC		LTR:CKY/MSEVKA:CMC RESPONSE/ CMC SUBMISSION WAS SENT TO THE FDA, THESE ARE COMMENTS FROM THE FDA REVIEW THAT WAS RECEIVED 4/23/96 (DATED 4/18/ 96). AEF

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96/04/29	20-625:960429	FDA Tel	Clinical		CONTACT:BBONO/BA:PJPR0007/ TWO QUESTIONS WERE RECEIVED FROM BBONO REGARDING THE ANALYSIS OF QTC IN PJPR0007. AEF
96/04/30	20-625:960430	MMD Ltr	CMC		DESK COPY 4/26/96 RESPONSE/ DESK COPY TO GSTRANGE OF SUBMISSION DATED 4/26/96 ADDRESSING THE CMC IR LETTER OF APRIL 18, 1996 (FAXED 4/23/96) LJG
	20-625:960430A	FDA Tel	Clinical Other		CONTACT:HSEVKA/CKY:MAPPING/ SEVKA CALLED REGARDING THE MAPPING OF DOUBLE DIPPERS. FDA THOUGHT THEY COULD THIS WITH THE INFO FROM THE REPORTS BUT ARE HAVING A DIFFICULT TIME. AEF
96/05/02	20-625:960502	MMD Sub	Clinical		RESPONSE TO FDA REQUEST/ REF: FDA REQUESTS OF APRIL 25, 27, & 30, 1996 REGARDING CLARIFICATION OF COMPLI- ANCE AND PATIENT ACCOUNT IN STUDIES PJPR0009, 010, 023, 024, AND 017. NOTE: ATTACHMENT FOR DR SEVKA ONLY-PREVIOUSLY SUBMITTED MATERIAL. LJG
	20-625:960502A	MMD Tel	Other		CONTACT:CKY/JJENKINS:DEAR DR/ CINDY PHONED JOHN JENKINS IN AN EFFORT TO CONFIRM THE REQUEST PLACED BY DR. SEVKA FOR A DEAR DOCTOR LETTER. AEF COPY OF DATA FROM 18-949:960502B
96/05/06	20-625:960506	FDA Tel	Labeling		PHONE:HSVEKA/JHN/ANALYSIS ADR/ PHONE CONTACT:HSVEKA/JHN/NEEDS AN ANALYSIS ON THE ADRS AND LABORATORY VALUES ON 60 YR OLD AGE GROUP.
96/05/07	20-625:960507	MMD Tel	CMC Other		FOLLOW-UP ON EA SECTION/ CONTACT: DSHAH/HSAGER: FOLLOW-UP ON EA SECTION QUESTIONS.

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96/05/07	20-625:960507A	NMD Tel	CMC		FOLLOW UP ON QUESTION/ CONTACT; DSHAH/BROGERS: FOLLOW UP ON A QUESTION FROM THE CSO (RECEIVED BY CINDY KIRK-YOURTEE) ON THE DRUG PRODUCT STABILITY.
	20-625:960507B	FDA Tel	Clinical		CONTACT:GSTRANGE/CKY:REQUEST/ GRETCHEN CALLED TO REQUEST THE REPORT WITH 18 MONTH STABILITY DATA REFERENCED IN OUR RECENT CMC SUBMISSION. AEF
96/05/09	20-625:960509	NMD Sub	CMC		CMC:RESP TO REQ OF 5/7/96/ REF: TELEPHONE REQUEST 5/7/96 18-MONTH STABILITY DATA - DUPLICATE DISKETTES SENT. LJG
	20-625:960509A	FDA Tel	Clinical		CONTACT:BBONO/BA:PJPR0007/ BARBARA BONO CALLED TO SEE IF WE COULD REVIEW A DRAFT OF A PORTION OF HER REVIE
	20-625:960509B	FDA Tel	Labeling		OF THE STATS ANALYSIS. AEF CONTACT:MSEVKA/CKY:DEAR DR LTR/ SEVKA TELEPHONED TO INFORM CINDY THAT THE DEAR DR LETTER WAS SATISFACTORY WITH ON EXCEPTION OF ONE MINOR ELEMENT. AEF
	20-625:960509C	FDA Fax	Clinical		COPY OF DATA FROM 18-949:960509 FAX:BBONO/BA:PJPR0007/ BARBARA BONO SENT FAX TO BOB AHLBRANDT COMMENTS TO PJPR0007. AEF
96/05/10	20-625:960510	NMD Sub	Clinical		RESPONSE TO 5/6/96 REQUEST/ RESPONSE TO 5/6/96 REQUEST FOR SUMMARIES FOR ADVERSE EVENTS AND CLINICAL LABORATORY DATA FROM THE ADEQUATE AND WELL CONTROLLED STUDIES IN SUBGROUPS BY PATIENT AGE. LJG

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96/05/14	20-625:960514	MMD Tel	Clinical Labeling Other		CONTACT:CKY/MSEVKA:MISC/ CINDY AND TANYA RUSSELL PHONED SEVKA TO TO DISCUSS HIS REQUEST ON SKIN WHEAL AND FLARE DATA. ALSO DISCUSSED WAS THE DEAR DOCTOR LETTERS. AEP
96/05/15	20-625:960515	MMD Sub	CMC		HARD COPY OF DATA SENT 5/9/95/ TO PROVIDE A HARD COPY OF DATA PROVIDED ON DISKETTES WITH 18-MONTH STABILITY DATA ON DRUG PRODUCT IN (I) EXCEL SPREAD SHEET (FILE FE18.XLS) AND (II) ASCII SPACE DELIMITED FILE (FILE FE18.TXT) SUBMITTED ON MAY 9, 1995. LJG
96/05/16	20-625:960516	FDA Tel	CMC		CLARIFICATION ON RESPONSE/ CONTACT: DSHAH/CBERTHA: CLARIFICATION ON RESPONSES.
96/05/21	20-625:960521	FDA Tel	Other		CONTACT:GSTRANGE/CKY:MESSAGE/ GRETCHEN CALLED TO INFORM CINDY THAT SHE HAD A MESSAGE FOR PAUL MEIHOUSE, THEY NEVER GOT THE 2/16 SUBMISSION. AEP COPY OF DATA FROM 48,486:960521A
96/05/22	20-625:960522	FDA Ltr	CMC		LTR:GSTRANGE/CKY:EA REVIEW/ RECEIVED LETTER THAT FDA HAS FINISHED REVIEW OF EA SECTION. AEF
96/05/23	20-625:960523	FDA Tel	CMC		REVIEWING STABILITY DATA/ CONTACT: DSHAH/BBONO: REVIEWING STABILITY DATA.
	20-625:960523A	MMD Tel	CMC		CMC & BIOPHARM RECOMMENDATIONS/ CONTACT: DSHAH, CKIRK-YOURTEE, RJORDAN, PSKULTETY, TROSANSKE, CLINDSEY, DYU / CBERTHA, GSTRANGE, BGILLESPIE: DISCUSS CMC & BIOPHARM RECOMMENDATION.
	20-625:960523B	MMD Fax	Clinical		FAX:CKY/GSTRANGE:MEETING/ SENT FAX TO GRETCHEN RE: TABLES FOR MEETING
96/05/28	20-625:960528	MMD Sub	Ad/Promo		REQUEST FOR REVIEW OF AD/ REQUEST FOR REVIEW OF ONE-PAGE "COMING SOON" AD IN SUPPORT OF ALLEGRA. LJG

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96/05/30	20-625:960530	MHD Ltr	Other		GEN CORR: NAME CHANGE/ AS RESULT OF 6/95 ACQUISITION OF MHD BY HOECHST CORP,, MHD IS NOW KNOWN AS HOECHST MARION ROUSSEL, INC.
	20-625:960530A	MHD Fax	Clinical CMC Other		FAX:CKY/MSEKVA:MULT ISSUES/ CINDY SENT SEVKA A FAX IN RE: TO DEAR DR LETTER, THE SAFETY UDPATE AND PROTOCOLS 27 AND 31. RESPONSE TO DR. JENKINS EA REQUESTS. AEF
	20-625:960530B	MHD Fax	Other		COPY OF DATA FROM 18-949:960530 FAX:CKY/GSTRANGE:ATTENDEES/ CINDY FAXED GRETCHEN A LIST OF ATTENDEES THAT WERE AT THE MAY 23, 1996 MEETING (CMC RESPONSE). AEF
96/05/31	20-625:960531	MHD Sub	Other		RESPONSE TO FDA REQUEST 5/22/ RESPONSE TO FDA REQUEST OF 5/22/96 RE: EA CERTIFICATION AND COMPANY NAME CHANGE LJG
	20-625:960531A	FDA Fax	CMC		FAX:BROGERS/CKY:CMC REVIEW QUE/ BRIAN D ROGERS SENT CINDY FAX OF CMC QUESTIONS (FDA RESPONSE TO OUR SUBMISSION APRIL 26, 1996) AMENDMENT. AEF
	20-625:960531B	MHD Fax	Ad/Promo		FAX:PLA/JHANKIN/PRECLEARANCE/ FAX:PLA/JHANKIN/PRECLEARANCE ON A "COMING SOON" ADD FOR ALLEGRA 60MG CAPSULES. REVIEWED WITH NO OBJECTIONS.
	20-625:960531C	FDA Ltr	Ad/Promo		LTR:PLA/JHANKIN/PRECLEARANCE/ LTR:PLA/JHANKIN/PRECLEARANCE ON A "COMING SOON" AD FOR ALLEGRA 60 MG CAPSULES. NO OBJECTIONS.
96/06/03	20-625:960603	MHD Sub	CMC		RESP TO REQ: SAS DATASET/ RESPONSE TO REQUEST BY DR B. BONO OF SAS DATASET ON THE 18-MONTH STABILITY OF FEXOFENADINE HCL CAPSULES. DISKETTE PLUS HARD COPY PROVIDED. LJG
96/06/04	20-625:960604	MHD Fax	CMC		FAX:CKY/GSTRANGE:ATTENDEES/ CINDY FAXED GRETCHEN LIST OF ATTENDEES AT TODAY'S MEETING ON CMC LETTER. AEF

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96/06/04	20-625:960604A	MMD Sub	Clinical		FINAL SAFETY UPDATE/ 28 VOLUMES COMPRISED OF REPORTS FOR STUDIES WHICH WERE COMPLETED BETWEEN THE DATE CUT-OFF PERIOD FOR NDA SUBM. AND 5/15/96 - PJPR0027, PJPR0031, AND PJPR0045. LJG
	20-625:960604B	MMD Tel	CMC		DISCUSS RESPONSE TO QUESTIONS/ CONTACT: DSHAH, CKIRK-YOURTEE, DYU, DPETERSON, TVEYSOGLU, DHENTON/BROGERS, CBERTHA, GSTRANGE: DISCUSS RESPONSE TO ORIGINAL SET OF QUESTIONS DATED 4/18/96. SHARE ADDITIONAL INFORMATION/ CONTACT: DSHAH/BROGERS, CBERTHA: SHARE ADDITIONAL INFORMATION AFTER TELECONFERENCE.
	20-625:960604C	MMD Tel	CMC		
96/06/05	20-625:960605	FDA Tel	CMC		CLARIFY ISSUES/ CONTACT: DSHAH/BROGERS: CLARIFY AN ISSUE ON TOTAL IMPURITIES. FAX:GSTRANGE/CKY:PACK INS COMM/ GRETCHEN SENT FAX OF PRELIMINARY FDA COMMENTS ON THE DRAFT PACKAGE INSERT SUBMITTED WITH THIS NDA. AEF
	20-625:960605A	FDA Fax	Labeling		
	20-625:960605B	MMD Tel	CMC		CONTINUE DISCUSSIONS/QUESTIONS/ CONTACT: DSHAH/CBERTHA: CONTINUE DISCUSSIONS, DISCUSS FDA REQUESTS.
96/06/06	20-625:960606	MMD Sub	Clinical		DESK COPIES OF 6/4/96 SUBM./ DESK COPIES OF TEXT ONLY (VOLS 1, 2, 9, 28) OF THE FINAL SAFETY UPDATE WHICH WAS SUBMITTED ON 6/4/96.
	20-625:960606A	MMD Ltr	CMC		RESPONSE TO FDA: CMC ISSUES/ RESPONSE TO COMMENT 6.D OF FDA 4/18 LTR AND RE: HMR WISHES TO WITHDRAW REYNOLDS METALS CO AS SUPPLIER OF ALUM FOIL/VINYL HEAT SEAL COATING BACKING MATERIAL. RESPONSE TO COMMENT 6.D PROVIDED ON EXCEL SPREADSHEET ON DISKETTE. LJG
	20-625:960606B	FDA Tel	CMC		CONTACT:BROGERS/CKY:FOLLOW-UP/ BRYAN ROGERS CALLED TO FOLLOW-UP TO DISCUSSIONS WITH DHIREN SHAH. AEF
	20-625:960606C	MMD Tel	CMC		SPECIFIC SURFACE AREA SPEC/ CONTACT: DSHAH/BROGERS: DISCUSS SPECIFIC SURFACE AREA SPEC

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96/06/07	20-625:960607	NMD Sub	CMC		FULL RESPONSE TO ROGER'S QUEST/ RE: DR ROGER'S REQUEST OF 5/31 AND OUR 4/26 CMC AMENDMENT: FULL RESPONSE TO QUESTIONS AND A COPY OF CONFIRMATION OF DHF DEFICIENCY WHICH HAS BEEN RESOLVED BY LAWSON MARDON PACKAGING. LJG
96/06/11	20-625:960611	FDA Tel	CMC		DISCUSS RESPONSES/ CONTACT: DSHAH/BROGERS: DISCUSS RESPONSES.
96/06/12	20-625:960612	NMD Tel	CMC		MIDLAND BPR/ CONTACT: DSHAH/BROGERS; DISCUSS MIDLAND BPR.
	20-625:960612A	FDA Tel	CMC		REQUEST A DRAFT LSIT/ CONTACT: DSHAH/BROGERS: REQUEST A DRAFT LIST OF ANY PHASE 4 COMMITMENTS WE HAVE MADE IN THE CMC AREA.
	20-625:960612B	FDA Tel	CMC		LACKING STABILITY INFORMAION/ CONTACT: MORTYL/BROGERS: STABILITY PROTOCOL IS LACKING INFORMATION.
96/06/13	20-625:960613	FDA Tel	CMC		PROVIDE UPDATED STABILITY/ CONTACT: DSHAH/CBERTHA: PROVIDE UDPATED STABILITY PROTOCOL FOR THE DRUG PRODUCT.
	20-625:960613A	NMD Tel	CMC		FOLLOW UP ON EARLIER CONTACT/ CONTACT: DSHAH/CBERTHA: FOLLOW UP ON EARLIER CONTACT - MODIFIED STABILITY PROTOCOL.
96/06/14	20-625:960614	NMD Fax	Clinical		FAX:CKY/BROGERS:CORRECT WORD/ CINDY SENT FAX TO BRYAN ROGERS TO INSERT THE WORD "ONLY" TO THE STABILITY PROTOCOL UNDER POINT #2 PER HIS REQUEST. AEF
	20-625:960614A	NMD Sub	CMC		LTR:CKY/GSTRAUGE:CMC RESPONSE/ SENT IN ANOTHER RESPONSE ON CMC ISSUES THAT FDA REQUESTED. AEF
	20-625:960614B	NMD Fax	CMC		FAX:CKY/GSTRAUGE:CMC RESPONSE/ THIS IS FAX OF CMC RESPONSE. OFFICIAL COPY SUBMITTED VIA FEDEX. AEF

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96/06/14	20-625:960614C	FDA Tel	CMC		PROVIDE LITERATURE/ CONTACT: DSHAH/GARAS: PROVIDE LITERATURE OR TEXT BOOK REFERENCE TO THE WEIGHT TOLERANCE LIMIT CALCULATION.
	20-625:960614D	FDA Tel	CMC		UNACCEPTABLE WORDING/ CONTACT: DSHAH/CBERTHA AND BROGERS: UNACCEPTABLE WORDING IN RESPONSE.
	20-625:960614E	NMD Fax	CMC		FAX:CKY/GSTRANGE:CMC RESPONSE/ CINDY SENT COURTESY FAX OF CMC RESPONSE TO GRETCHEN TO HAND DELIVER TO BRYAN ROGERS. AEF
96/06/17	20-625:960617	FDA Tel	CMC		ANALYTICAL METHODS VALIDATION/ CONTACT: DSHAH/BROGERS: UPDATED ANALYTICAL METHODS VALIDATION PACKAGE MUST BE RECIEVED BY FDA BY FRIDAY (6/21)
96/06/18	20-625:960618	NMD Ltr	Clinical		RESPONSE TO FDA 6/10/96 REQUES/ REF: TO FDA JUNE 10, 1996 REQUEST: TABULATIONS AND APPENDICES FOR STUDY REPORTS EQUIVALENT; ECGS AVAILABLE FOR INTERIM PJPR0027 REPORT. LJG
	20-625:960618A	NMD Fax	Labeling		FAX:CKY/GSTRANGE:REF 6/5 FAX/. FAXED COPY OF SUBMISSION BEING MAILED TODAY - RESPONSE TO JUNE 5, 1996 FDA DRAFT LABLEING COMMENTS. LJG
	20-625:960618B	NMD Sub	Labeling		RESP TO 6/5 LABELING COMMENTS/ COMMENTS AND LABELING RECOMMENDATIONS AS ASSOCIATED WITH 6/5/96 FDA DRAFT PROPOSAL FOR LABELING. FAXED COPY SENT TO GSTRANGE. LJG
	20-625:960618C	NMD Ltr	Clinical		RESP TO 6/14/96 FDA REQUEST/ RESPONSE TO FDA REQUEST OF 6/14/96 CASE REPORT FORMS FOR ALL PATIENTS WHO REPORTED SYNCOPE AS AN ADVERSE EVENT. LJG

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96/06/19	20-625:960619	FDA Tel	Clinical		CONTACT:BBONO/BA:PJPR0007/ BARBARA BONO TELEPHONED BOB AHLBRANDT REFERENCING A PREVIOUSLY SUBMITTED ANALYSIS OF THE CORRELATION BETWEEEN QTC MEASUREMENTS AND FEXO PLASMA CONCENTRATI ONS FROM PROTOCOL PJPR0007. AEF
96/06/20	20-625:960620	NMD Sub	CMC		SUBMIT METHODS VALIDATION UPDA/ RESPONSE TO FDA REQUEST OF 6/14/96 FOR UPDATED METHODS VALIDATION PKG. CONSISTS OF 2 VOLUMES. LJG
	20-625:960620A	NMD Fax	Clinical		FAX:CKY/MSEKVA:PJPR0027/ CINDY SENT COURTESY FAX TO SEVKA FOR CRFS FOR PATIENT PJPR0027-PJST0206-0010 HARD COPY ALSO SENT VIA FEDEX. AEF
96/06/21	20-625:960621	NMD Sub	Clinical		RESP TO 3 FDA REQUESTS/ REF TO REQUESTS OF JUNE 14, 20 & 21. CASE REPORT PJPR0027 PJST0206 010 AND ECGS FOR 4 OTHER STUDIES. SUMMARY OF ADVERSE EVENTS FOR 6 PATIENTS. CLARIFI- CATION OF THE TERM "SAFETY EVALUABLE" PROVIDED. LJG
	20-625:960621A	FDA Tel	Clinical		CONTACT:BBONO/BA:PJPR0009/ BOB RECEIVED A CALL FROM BARBARA BONO RE: SEEKING CONFIRMATION OF HOW SIX PATIENTS THAT WERE UNBLINDED INCORRECTLY IN PROTOCOL PJPR0009. AEF
	20-625:960621B	NMD Fax	Clinical		FAX:BA/BBONO:PJPR0009/ BOB FAXED BARBARA BONO INFORMATION ON PJPR0009 FOR THE SIX PATIENTS WITH INCORRECT TREATMENT ASSIGNMENTS. AEF
	20-625:960621C	NMD Fax	Clinical		FAX:CKY/MSEKVA:SAFETY EVALUABL/ CINDY SENT COURTESY FAX OF SUBMISSION (SENT VIA FEDEX) OF EXPLANATION OF TERMI NOLOGY FOR SAFETY EVALUABLE. AEF
96/06/25	20-625:960625	FDA Tel	CMC		VERIFY SUBMITTED INFORMATION/ CONTACT: DSHAH/CBERTHA: VERIFY SUBMITTED INFORMATION.
	20-625:960625A	FDA Fax	Labeling		FAX:GSTRANGE/CKY:LABELING/ GSTRANGE SENT FAX RE: COMMENTS ON THE LABELING (12 PAGES). AEF

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96/06/25	20-625:960625B	FDA Tel	CMC		FOLLOW-UP 60 CT PACKAGES/ CONTACT: DSHAH/CBERTHA: FOLLOW-UP TO EARLIER CONTACT REGARDING 60-COUNT BRACKETED BETWEEN THE 30 AND 100/500 COUNT PACKAGES.
96/06/26	20-625:960626	NMD Sub	Labeling		RESPONSE TO FDA REQUEST/ PER CONVERSATION OF 6/26 - SUBMITTED CARTONS AND LABELS AS REQUESTED. LJG
96/06/27	20-625:960627	NMD Fax	Labeling		FAX:CKY/GSTRANGE:LABELING FAX/ CINDY FAXED THE LABELING SUBMISSION TO GRETCHEN. HARD COPY SENT VIA FEDEX, THE FAX COPY IS COUTESEY TO GRETCHEN. AEF
96/07/09	20-625:960709	NMD Fax	Labeling		FAX: LABELING COMMITMENT/ REF TO TELEPHONE CALL 7/9/96 - CHANGES REGARIND THE ADDITIONAL MOISTURE STATEMENT IN PKG COMPONENTS (TO INCLUDE TRAYS, BOTTLE LABELS AND CARTONS) IMMEDIATELY FOLLOWING LAUNCH. LJG
	20-625:960709A	NMD Sub	Labeling		SUBMIT LABELING COMMITMENT/ REF TO TELEPHONE CALL OF 7/9/96 REGARD-LABELING - TO IMPLEMENT CHANGES REGARD-ING THE ADDITIONAL MOISTURE STATEMENT IN PKG COMPONENTS (TO INCLUDE TRAYS, BOTTLE LABELS AND CARTONS) IMMEDIATELY FOLLOWING LAUNCH.
96/07/11	20-625:960711	NMD Sub	ALL		APPLICABILITY OF 5-YR EXCLUSIV/ REQUEST AGENCY UPON APPROVAL OF NDA GRANT FEXOFENADINE FIVE YEARS OF NON-PATENT EXCLUSIVITY. LJG
96/07/17	20-625:960717	NMD Sub	Ad/Promo		PROMO LAUNCH FOR PRECLEARANCE/ PROMOTIONAL LAUNCH ITEMS SUBMITTED FOR REVIEW AND PRECLEARANCE AND NEAR-FINAL DRAFT PRESCRIBING INFORMATION. LJG

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96/07/18	20-625:960718	MMD Tel	Labeling		CONTACT:PLA/JHANKIN/PROMO SUB/ PHONE:PLA/JHANKIN/FOLLOW-UP ON PROMOTIONAL SUBMISSION SENT BY SPECIAL COURIER
96/07/24	20-625:960724	MMD Sub	Ad/Promo		ADD'L CLARITY ON REFERENCES/ RESPONSE TO VOICEMAIL REQUEST OF 7/23/96 ADDITIONAL CLARITY ON REFERENCES OF THE PROMOTIONAL LAUNCH ITEMS. LJG
	20-625:960724A	FDA Fax	Labeling		FAX:GSTRANGE/PLA:LABELING CHAN/ GRETCHEN STRANGE FAXED FINAL CHANGES TO ALLEGRA LABELING TO PEG. WANTS RESPONSE TO "AGREE" OR "NOT AGREE" BY 7/25/96 AM. AEF
	20-625:960724B	MMD Fax	Ad/Promo		FAX: COPY OF SUBMISSION SENT/ FAXED COPY TO JHANKIN OF SUBMISSION BEING SENT ON PROMOTIONAL LAUNCH ITEMS - ADDITIONAL CLARITY ON REFERENCES. LJG
96/07/25	20-625:960725	MMD Fax	Labeling		FAX:PLA/GSTRANGE:LABELING/ PEG FAXED GRETCHEN STRANGE OUR VERSION OF THE LABELING THAT FDA REQUESTED BE CHAGED FROM FAX OF 7/24/96. AEF
	20-625:960725A	MMD Fax	Labeling		FAX:PLA/GSTRANGE:CORRECTED PAG/ THERE WAS A TYPOGRAPHICAL ERROR IN THE FINAL DRAFT THAT WAS SENT TO FDA. PEG FAXED THE CORRECTED VERSION TO GRETCHEN STRANGE. AEF
	20-625:960725B	FDA Fax	ALL		FAX:GSTRANGE/CKY:APPROVED NDA/ RECEIVED FAXED VERSION OF APPROVED LETTER FOR ALLEGRA FROM GRETCHEN STRANGE. AEF
	20-625:960725C	FDA Fax	Labeling		FAX:FDA RESP TO 7/17 REQUEST/ RE: MACMIS ID#4470 - FDA RESPONSE TO 7/17/96 REQUEST FOR COMMENTS CONCERNING PROMOTIONAL LAUNCH MATERIALS. COMMENTS AND RECOMMENDATIONS. LJG

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96/07/25	20-625:960725D	MMD Fax	Ad/Promo		FAX:PLA/HANKIN:LTR+EXHIBIT 1/ PLA FAXED TO JHANKIN COPY OF LETTER AND EXHIBIT #1 SENT BY FEDEX 7/24/96 - PROMOTIONAL LAUNCH ITEMS - ADDITIONAL CLARITY ON REFERENCES. LJG
	20-625:960725E	MMD Sub	Labeling		SUBMIT FINAL DRAFT PI/ RESPONSE TO FDA REQUEST - SUBMIT FINAL DRAFT PRESCRIBING INFORMATION WHICH INCORPORATES RECOMMENDATIONS FROM 7/24 FAX AND CONVERSATION 7/25. LJG
	20-625:960725F	FDA Ltr	Ad/Promo		LTR:JHANKIN/PLA/PROMO LAUNCH/ LTR:JHANKIN/PLA/ORIGINAL LTR CONCERNING PROMOTIONAL LAUNCH MATERIALS FOR ALLEGRA
96.07 29	20-625:960729	MMD Fax	Ad/Promo		FAX:PLA/JHANKIN: RESPONSE 7/25/ FAX OF SUBMISSION BEING SENT FEDEXP
	20-625:960729A	MMD Sub	Ad/Promo		PROMOTIONAL LAUNCH ITEMS - RESPONSE TO 7/25/96 PRELIMINARY COMMENTS. MACMIS ID #4470. LJG RESPONSE TO 7/25 PROMO LAUNCH/ SUBMISSION OF RESPONSE TO 7/25/96 PRELIMINARY COMMENTS ON PROMOTIONAL LAUNCH ITEMS MACMIS ID#4470. LJG
96.07 30	20-625:960730	MMD Fax	Clinical		FAX:CKY/GSTRANGE:POLLEN COUNTS/ CINDY FAXED THE FDA POLLEN COUNTS FROM APPENDIX L1 FROM THE PJPR0017 REPORT AT THE FDA'S REQUEST. AEF
	20-625:960730A	MMD Fax	Clinical		FAX:PLA/JHANKIN:FAX TO SEVKA/ PADAMS FAXED TO JHANKIN COPY OF FAX CKIRK SENT TO MSEVKA RE: RESPONSE TO REQUEST FOR POLLEN COUNTS THE LISTINGS FROM APPENDIX L1 FROM PJPR0017 REPORT. LJG

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96 07 31	20-625:960731	MMD Ltr	ALL		LTR:CKIRK/STRANGE: SOFTWARE/ REF: MEETING WITH SEVKA AND BONO 7/26 WHERE SOFTWARE REQUIREMENTS WERE IDENTIFIED. MATERIAL SENT AS REQUIRED BY DEBORAH STALEY. LJG
	20-625:960731A	FDA Fax	Ad/Promo		FDA COMMENTS RE: PROMO LAUNCH/ FAXED COPY OF LETTER FROM FDA - RESPONSE TO HHR 7/17/96 REQUEST FOR COMMENTS ON PROMOTIONAL LAUNCH MATERIALS - THIS LTR SUPPLEMENTS DDMAC'S 7/25 COMMENTS ON PROPOSED PRESS KIT MATERIALS AND COMMENT ON PROPOSED DIRECT-TO-CONSUMER TV SCRIPT AND STORYBOARD. LJG
	20-625:960731B	MMD Tel	CMC		CONTACT: CAPSULES FOR COMMERCE/ CONTACT: DSHAH/CBERTHA: FOLLOW UP ON DISCUSSIONS ABOUT ISSUE OF ALLOWING 8 LOTS OF CAPSULES BE DISTRIBUTED FRO COMMERCE.